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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

NORTHERN IRELAND, GOVERNMENT OF: MINISTRY OF HEALTH AND LOCAL GOVERNMENT. **Report on Health and Local Government Administration in Northern Ireland during the Year ended 31st December, 1959.** Cmnd. 420. pp. viii + 95, 4 graphs. 1960. Belfast: H.M. Stationery Office. [5s. 6d.]

This Annual Report follows the line set by its predecessor [this *Bulletin*, 1960, v. 35, 413].

In the introduction by Dr. Frank M. MAIN, the Chief Medical Officer, it states that it is proposed in future to model this section on that of the annual report of the Chief Medical Officer of the Ministry of Health of England and Wales and make it an appraisal of the "State of the Public Health" in Northern Ireland.

The natural increase of the population was 15,403 but as the estimated increase of the population during the year (making 1,407,700), was only 5,400 the net emigration was considerable. The birth rate was 21·9 per 1,000 population and the death rate 10·9. The infant mortality was 28·4, and the stillbirth rate 23 per 1,000 total births; the maternal mortality was 0·58 per 1,000 live births. The tuberculosis death rate at 10·2 per 100,000 population was the lowest ever recorded and is 7% lower than in 1958: the notifications of respiratory tuberculosis fell by 16% and of non-respiratory by 22%. Diseases of the cardiovascular system accounted for about 35% of all deaths. The results of a departmental enquiry into deaths attributable to coronary thrombosis showed, however, that in only 56% could this diagnosis be accepted as proved. Deaths from bronchial carcinoma are increasing slightly and the rate is now 24·6 per 100,000 population: this being a little more than half the rate in England and Wales. The bronchitis death rate at 40 per 100,000 population is also substantially lower than in England and Wales.

There was no death from poliomyelitis and only 22 cases (16 paralytic) were notified: the type of virus found was almost entirely type 1 compared with type 3 in 1958: in 4 cases virus of the ECHO/Coxsackie strains of the enteric viruses was isolated, and in one fatal case of encephalitis type 1 poliovirus was recovered.

There was an outbreak of typhoid fever with 29 cases.

The mass vaccination of newly born babies with BCG has been discontinued.

The Hospital and Specialist Services continue to be administered by a special Board. Its estimated expenditure during 1959/60 was £14,205,000 of which £2,715,000 was for capital purposes: these figures exceed those for the actual costs in 1958/59 by £1,360,280 and £209,057. The number of beds available at the end of the year was 16,274 and the admissions during the year were 145,656. A new hospital of 394 beds at Altnagelvin is the first completely new hospital to be built in the United Kingdom since the war. The number of specialists in posts, which was about 140 in 1948, is now 323 and they are spread better throughout the province. The shortage of junior medical staff continues.

There is a full report on the mental health services. There were more admissions to mental hospitals; 4,976 in 1959, 4,588 in 1958: a higher percentage were voluntary admissions and there were more discharges; 4,266 in 1959, 3,843 in 1958: the recovery rate was 32·63% compared with 31·45% in 1958. More psychiatric out-patient departments are being opened and a day hospital is being provided.

Persons "requiring special care" are those formerly called mentally defective: the total number known to the department at the end of 1959 was 3,517, of whom 1,668 were in institutions (763 in mental hospitals).

There were 742 doctors providing general medical services, of whom 372 "practise in partnership". Their lists are inflated and the total number on them exceeds the population of the province.

The costs of the general dental, the pharmaceutical and the supplementary eye services are all slowly rising. Drugs now cost 38s. 3d. per patient.

There were 10,282 domiciliary confinements. The number of ante-natal clinics is 38 and the midwives pay many home visits. The number of child welfare clinics is 193 and about 60% of the children are taken to them regularly. There are still vacancies in the establishment of health visitors though the number working full time increased during the year by 33: many are receiving

instruction in the care of mental patients in the community.

73% of the infants were vaccinated against smallpox. There is an active campaign to obtain volunteers to be vaccinated against poliomyelitis, but there is increasing difficulty in obtaining consent to immunization against diphtheria.

The School Health Service continues much as before and it is stated that " a free National Health Service does not make the School Health Service unnecessary ".

There are 1,538 persons in the care of the Welfare Authorities: 90% were of pensionable age of whom 46% were infirm or handicapped.

During the year 4,894 houses were built; almost the same as in the previous year: 2,000 of them were built privately for owner occupation and attracted a subsidy from public funds. Slum clearance and redevelopment are proceeding as is the fairly new scheme to subsidize the conversion of large houses into smaller units. There is an interesting chapter on town and country planning.

[This report is comprehensive but unspectacular and shows evidence of a solid year's work.]

Allen Daley

PETROVIC, B. **The Public Health Service in Yugoslavia.** 69 pp., 38 figs., 1 diagram & 1 chart. 1958. Belgrade.

This is a good description of the public health services of Yugoslavia as they have been developed in the 12 years since liberation, and is primarily for the benefit of foreign visitors.

Yugoslavia is a federation of 6 republics: it contains 95 districts and 1,193 municipalities. The supreme governing body is the Federal People's Assembly, which is bicameral and appoints an Executive Council of 35 members under the presidency of the President of the Republic. The Executive Council contains political members from each republic. There is a Federal Board of Social Welfare and Public Health containing medical experts. Each of the 6 republics has its own Assembly and Executive Council and appoints a Public Health Council: there are also Public Health Councils for districts and municipalities.

There is a compulsory scheme of health insurance for all employees and for many other groups there is free medical treatment for all illnesses or for specified ones such as tuberculosis, mental diseases or cancer. Others are required to pay for treatment but their numbers become smaller each year and consideration is being given to a universal free medical service.

The population of Yugoslavia is about 18 million: by Western standards it is a young country and only 5·6% of the population are over 65 years. Compared with 1939 there have been spectacular increases in the number of, and attendances at, " advisory centres " for women and children and in the number of beds for maternity cases. Instruction is given in contraceptives, and abortion, except for medical or social reasons, is illegal—nevertheless, illegal abortions do occur. Infant mortality has a wide range in different parts of the country and in 1956 the Federal rate was 98·3 per 1,000 live births.

Prevalent infectious diseases are measles, whooping cough, scarlet fever, typhoid fever and dysentery, but typhus and relapsing fevers have been stamped out. In 1938 the death rate from tuberculosis was 199 per 100,000 of the population: in 1955 it was 75. Anti-tuberculosis dispensaries now number 202 and there are 18,000 hospital beds for the tuberculous. 10 million people have been tested with tuberculin and over 4 million vaccinated with BCG.

The steps taken to control malaria, trachoma, endemic syphilis, fungal diseases of the skin, nutritional diseases, industrial accidents and cancer are well described.

Destruction of property during the war and industrialization of more recent date have presented many health problems. Water supplies and sewage disposal plants have been provided and factory owners are required to contribute 10% of their wages bills to a fund to provide houses for the workers.

Laboratory and advisory services are provided in 10 institutes of hygiene and 51 public health centres.

There are 71,601 hospital beds (4·01 per 1,000 population) which are about double the figures for 1939. The number of out-patient departments and polyclinics has increased from 1,165 in 1950 to 2,345 in 1956: factory health stations from 240 to 606 and dental clinics from 518 to 946. The Yugoslav Red Cross organizes propaganda and recruitment for the blood transfusion service. Much attention is paid to rehabilitation. The entire pharmaceutical service has been nationalized. There are numerous spas for climatic and physical methods of treatment.

Since 1956 a sanitary inspection service has been developed. More doctors and other health workers are needed and in the 12 years since liberation twice as many doctors have graduated as the total number at work in 1939. There is now one doctor per 1,620 of the population.

Health insurance funds provide 65% of the total outlay on the service; 20% comes from other public sources and 15% from private persons using the scheme: 3% of the insurance fund is set aside for preventive measures. The health services absorb 3·36% of the national revenue.

[This is a most informative and valuable publication in very good English.] *Allen Daley*

BACKETT, E. M. **Future Role of the Family Doctor.** *Lancet.* 1960, Nov. 12, 1075–6.

The author is Professor of Social Medicine in the University of Aberdeen.

The article deals with the changing pattern of disease from the infections to the chronic degenerative diseases. " The borderline between prevention and very early treatment is rapidly becoming meaningless." The new approach suggested is preventive " in the sense of using our growing epidemiological knowledge accurately to define vulnerable groups, families, and individuals in our population and of manipulating their personal and social environment to prevent disease ". No one likes other people to interfere with his set mode of life, yet to be effective the future general practitioner must meddle with such things and in an increasingly personal way.

Though the infections are declining they are not yet defeated and this throws into relief such things as the burden of chronic bronchitis which causes the loss of 25 million man-days a year, cancer with 100,000 deaths

a year, heart disease, diabetes and multiple sclerosis. There is, also, the waste of foetal and neonatal life.

The vulnerable age-groups are changing: so are the sex ratios and the type and duration of disease. In these circumstances "*prevention* acquires a new urgency, and the wise family doctor is being forced increasingly to switch his attention from sick people to the habits and behaviour of healthy people many years before the clinical onset of illness".

There is need to change the custom of medical advice being sought only when people feel ill, though the difficulties in interesting people in what *may* happen to them in 20 years is appreciated. The doctor now has "a growing armoury of screening devices and simple tests by which he can pick the already ill from among the merely vulnerable people in his practice, and so make . . . earlier diagnoses". As an illustration reference is made to the early diagnosis of cancer of the uterine cervix by looking for exfoliated cells, but the author asks pertinently how apparently healthy women can be induced to submit themselves for examination. The "new diseases are themselves forcing us into at least the contemplation of a different sort of medical care". We must, however, avoid creating a "mass fear of illness". The experience at Framingham in the U.S.A. suggests, however, "that these dangers can be avoided". *Allen Daley*

AMERICAN PUB. HEALTH ASS. **Public Health is One World. [Papers presented at 87th Annual Meeting, 1959.]** *Amer. J. Pub. Health.* 1960, June, v. 50, No. 6, Pt. 2, Suppl., 94 pp., 9 figs. [26 refs.]

This supplement to the *American Journal of Public Health* contains the text of papers read at the 87th Annual Meeting, 1959, and most of the contributors are from countries other than the United States. The general theme tends towards unification, but the papers themselves are very diverse. Dr. M. G. CANDAU sums up some of the work and problems of WHO, and Dr. J. F. C. CAMBOURNAC refers specifically to similar subjects as they relate to Africa. M. PATE discusses UNICEF and child health, and Dr. A. HORWITZ maternity and child health in the Americas and the programmes devised by governments and international organizations to cope with the still formidable difficulties. These 4 papers are conceived on general lines; they are important conspectuses of present-day conditions.

Dr. T. F. FOX describes the medical organization of modern China, where the political framework reaches out effectively to all the people, rural and urban, and carries with it a health component in which the practitioners of traditional medicine have an important part. The general impression is distinctly favourable, and this is also true of the impression conveyed by Dr. J. B. GRANT in his review of Western medicine in pre-Communist China compared with the situation as it now exists; the lag is being overcome at astonishing speed.

Professor A. A. SMORODINTSEV writes on the live vaccines against virus diseases now being used in the U.S.S.R. on a large scale, mentioning particularly the poliomyelitis, influenza and mumps vaccines, and ending with a remark on the hope that the extensive use of these vaccines in the Soviet Union will stimulate other countries to re-assess the risks involved (which are claimed to be slight) and the great benefits conferred. Dr. C. G. PANDIT gives an account of the newly recognized haemorrhagic virus diseases of Asia, especially Kyasanur forest disease, for which a vaccine prepared against Russian spring-summer encephalitis has been tried, but without much success.

Professor D. D. REID discusses cardio-respiratory disease as a field for international research; there are remarkable differences in recorded incidence in different countries, and it is obviously important to know whether doctors in those countries mean the same thing when their diagnostic labels correspond.

Miss E. MAGNUSSEN traces the development of home care plans in Denmark, which involve a home nursing service working in close contact with private practitioners.

Dr. M. S. ACKER describes the Saskatchewan comprehensive public cancer programme, under which all residents are entitled to diagnostic and treatment services at public expense. One result is earlier diagnosis and treatment of the disease affecting lip, skin and uterine cervix.

Dr. P. S. RAJULU examined the nose, throat and skin of dogs in a Kansas veterinary hospital, finding staphylococci in 94%, and concludes that pet dogs may be factors in the epidemiology of staphylococcal diseases of man.

Dr. Harvey FLACK draws attention to the change which has taken place in the findings reported for children medically examined in Britain 50 years ago and at the present time. Then one of the problems was undernutrition; now it is obesity.

Dr. M. YAMAGUCHI examines the population problem of Japan, and the policies adopted there which promote family planning. Dr. Brock CHISHOLM discusses even broader issues and the function of the United Nations in facing them, and the trend is not optimistic: "The greatest problems facing the world at this moment are getting almost no attention at all—such as food. We have no way of distributing food on a world basis. . . . There are hundreds of millions of people starving, but we have no method of feeding them". *Charles Wilcocks*

VITAL STATISTICS

MARTIN, W. J. **The Trend of Mortality since 1840.** *Med. Officer.* 1960, Nov. 4, v. 104, No. 19, 273–80, 1 fig.

Various aspects of mortality trends in England and Wales since 1841 are tabulated, described and discussed with particular reference to the validity of the statistics available for estimating the changes which have taken place in the pattern of mortality and to the medical, social, environmental and other factors which have brought about or influenced such changes. At ages 5–44 years in females and 5–24 in males death rates from all causes combined have steadily fallen since about 1841; in men aged 25–44 rates did not begin to decrease until about 1875 and at other ages until about 1901. At ages 15–19, 20–24, 45–54, 55–64 and 65–74 the female rates have decreased more rapidly than the male and the levels of the former are now only some 52–62% of those of the latter. Infant mortality has also fallen; in 1841–50 there were 167 and 137 deaths in the first year of life per 1,000 live births for males and females respectively compared with 30 and 23 per 1,000 in 1951–55. Expectation of life at birth has increased from 40·19 years for males and 42·18 years for females in 1841 to 67·85 for males and 73·53 for females in 1956–58.

After some observations on the trend of infant mortality, a variety of statistics are given in a series of short paragraphs dealing with cholera, smallpox, typhus and enteric fever. The annual influenza death rates from 1841–1957 are tabulated and discussed and the decline in mortality of children from diphtheria, scarlet fever, whooping cough and measles is shown graphically with observations in the text on the age incidence. Average annual age and sex specific death rates are shown for respiratory tuberculosis and non-respiratory tuberculosis for 1851–60, 1861–70, 1941–50 and 1951–55, and for all forms of pneumonia for 1861–70, 1871–80, 1941–50 and 1951–55. Similar data relating to cancer are discussed. [The table on cancer was inadvertently omitted and some cross references to subsequent tables are consequently wrong. The table has since been published in *Med. Officer*, 1960, v. 104, 326]. In amplification of these tables age and sex specific rates are shown for 1939–43, 1944–48, 1949–53 and 1954–58 for lobar pneumonia and bronchopneumonia separately and the average annual rates at all ages combined are given for specified cancer sites for 1948–57. Diseases of the circulatory system are not considered in detail because of the difficulties imposed on such an analysis by the changes in methods of classification of causes of death introduced in 1940.

This report is full of factual details about mortality trends which cannot be satisfactorily condensed. The content of the paper, as indicated in the preceding paragraph, makes it an excellent source of information for those who require a ready-made and competent appraisal of mortality changes over the last 100 years. The author's concluding paragraph is worth more publicity than it will probably get—he writes: "Public health enactments have now reached a stage when it is unlikely that further dramatic improvements in the health of the people can be attained by them. Although every advance produces new problems and perhaps the most pressing social need today is the care of the increasing number of old people in the population. Future advance in health depends more upon the individual conforming to the laws of hygiene than from action by the community".

E. A. Cheeseman

SIMPSON, J. **Mortality in Childhood.** *Med. Officer.* 1960, Nov. 4, v. 104, No. 19, 281–5, 3 figs. [18 refs.]

In 1851, 35·43% of the population of England and Wales were under the age of 15 years and 4·64% were aged 65 and over. By 1951 these proportions had become 22·25% and 10·94% respectively. Most of this change has taken place since about 1891 when the corresponding proportions, 30·64% and 5·21% respectively, were not very different from those of 1851. It is expected that by 1973 only 20·40% of the population will be under age 15 years and as much as 14·06% will be 65 and over. The birth and death rates tabulated for successive quinquennia from 1851–55 to 1946–50 exhibit general downward trends until 1936–40, although variations in the rate of decrease have occurred over the whole period. The decrease in the mortality rates since 1900 has been particularly large among infants and children. Infant mortality fell between 1901–05 and 1951–55 from 138 to 27 deaths in the first year of life per 1,000 live births. Between the same quinquennia the death rates per 1,000 population at ages 1–4, 5–9 and 10–14 years respectively fell from 50·2 to 6·19, 3·74 to 0·47 and 2·19 to 0·41.

Most of the decrease in infant mortality has occurred through a reduction in mortality after the first week of life. Thus a diagram shows that between 1928 and 1957 mortality in the first week of life has fallen only from about 22 to 18 per 1,000 live births. The same diagram shows the decline in the stillbirth rate from about 40 to about 20 stillbirths per 1,000 total births and focuses attention on the size of the problems of perinatal mortality which are yet to be solved. [This diagram shows stillbirth, infant and perinatal mortality rates on a common scale "deaths/1000 births" in a rather unconventional presentation, thus the above quoted rates can only be approximately expressed in the usual terms.]

The author discusses these changes in infant and childhood mortality with reference to work done elsewhere and attempts to compute the wastage through death in various age-groups (0–14, 15–64, and 65 and over in 1930–32 and 1955–57) in terms of the average number of potential years of life lost basing potential life on life table expectations. In this he follows the methods proposed by HERSCH (1944, *De la demographie actuelle à la demographie potentielle*, Geneva). At ages 0–14 for every 1,000 years of potential life it is estimated that 7·33 years were lost in 1930–32 compared with only 2·14 in 1955–57. At ages 15–64 the corresponding figures were 5·25 and 3·44 and at ages 65 and over, 43·92 and 43·29 respectively. Relatively this might be interpreted as a 70·81% improvement in the youngest age-group compared with 34.48% and 1·44% improvements at the intermediate and oldest age-groups.

E. A. Cheeseman

UTTLEY, K. H. **Infant and Early Childhood Death Rates over the Last Hundred Years in the Negro Population of Antigua, British West Indies.** *Brit. J. Preventive & Social Med.* 1960, Oct., v. 14, No. 4, 185–9.

The infant mortality of the coloured population of Antigua was fairly constant at 250 per 1,000 live births up to the beginning of the present century since when it has gradually fallen to 78. The infant mortality of England and Wales fell a litle faster during this period, from 145 to 36. The difference in the rate of fall is due to the post-neonatal rate. In Antigua the neonatal rate which was 50% above the rate in England and Wales is now only slightly in excess. The post-neonatal rate in Antigua is now one-third of the value of the early years while the rate in England and Wales is only one-fifth of its former size. The infant mortality in Antigua is still falling and there is nothing to suggest that the rate of fall is slowing down. The author suggests that a considerable improvement in infant mortality can be achieved by sanitary measures leading to a reduction in the mortality from infectious diseases and by social and economic measures leading to better nutrition and to a large improvement in the standard of child care. *W. J. Martin*

TOMASSON R. F. **Patterns in Negro-White Differential Mortality, 1930–1957.** *Milbank Memorial Fund Quarterly.* 1960, Oct., v. 38, No. 4, 362–86, 6 figs. [Refs. in footnotes.]

The national figures used in this enquiry have been supplemented by the experience of the Industrial Policy Holders of the Metropolitan Life Insurance Company because of alternating patterns in the official rates due to an artefact. For most causes of death the Negro population has a higher death rate than the white population. The largest part of the excess Negro mortality has been due to tuberculosis, influenza and pneumonia, diseases of the circulatory system and homicide. Considerable improvement has occurred during the past 30 years in the socio-economic well-being of the Negro and the gap between white and non-white has lessened. The object of this paper was to see whether the gap between the mortalities was decreasing or not. Since 1931 the age-adjusted death rates from all causes has fallen faster in the non-whites than in the whites, and the male rate has converged faster than the female. The white males in 1957 had higher age-adjusted death rates than the non-white males for only arteriosclerotic heart disease, cirrhosis of the liver and suicide. The only death rate among white females that exceeded the non-white rate was that of suicide. The racial differences in specific heart diseases may be due to a differential diagnosis. In recent years the infant mortality of the whites has fallen faster than that of the non-whites, and the non-white rate is now about 90% above the white rate compared with 60% in 1945. *W. J. Martin*

EPIDEMIOLOGY

RAJASTHAN. DIRECTORATE OF MEDICAL & HEALTH SERVICES [SHARMA, B. N., Director]. **Health Statistics 1959.** pp. viii + 120, 34 illustrations. 1960. Jaipur: Vital Statistical Section, Rajasthan, India.

The comparable volume for 1958 was reviewed in this *Bulletin*, 1960, v. 35, 330. The present report is considerably fuller than its predecessor, and includes a section in which information on vital statistics and other matters is given for the different Indian States in addition to Rajasthan. Other new items relate to health statistical indices, patients treated, and deaths certified by doctors.

There are evidently still great difficulties in collecting material. For instance in Table 3.6 the recorded infant death rate for the whole area varied from 40·4 per 1,000 live births in 1955 to 120 in 1959, and the rural rate from 2·9 in 1955 to 48·5 in 1958; no figures could be given for 1959. But the rate for urban areas varied much less—134·9 in 1955 to 154·5 in 1957 and 120 in 1959.

Nevertheless, the information is useful and its value will improve as time goes on; it is interesting to note that whereas in 1955 there was one doctor to 22,000 people, in 1959 there was one to 14,000.

Charles Wilcocks

RAJASTHAN. DIRECTORATE OF MEDICAL & HEALTH SERVICES [SHARMA, B. N., Director]. **Health Atlas 1959.** 47 mimeographed pp. of illustrations. 1959. Jaipur: Vital Statistical Section, Rajasthan, India.

In the introduction to this atlas Dr. SHARMA expresses the hope that it will be useful to health workers and those who are interested in assessing the health activities of the State. It should succeed in this.

It consists of a series of maps of the State and of its constituent districts, and diagrams on which are shown such things as vital statistics, immunization statistics, epidemiological figures, medical facilities and expenditure, and other relevant matters. The medical facilities include allopathic and traditional services.

The intention is evidently to display the information in a striking and pictorial way, and it is none the worse for this. The atlas is produced by a mimeograph process from typescript; later versions, perhaps, could be printed, with advantage. *Charles Wilcocks*

RAETTIG, H. Die Seuchenkurve. Methoden der Darstellung und Probleme der Ausdeutung. [**The Epidemic Curve. Methods of Representation and Problems of Interpretation.** *Arch. f. Hyg. u. Bakt.* 1960, May, v. 144, No. 3, 159–206, 26 figs. [77 refs.]

This review describes the different types of epidemic curves that can be observed. In an explosive epidemic arising from a single source in a large population it is shown that the primary cases have a binomial distribution.

The author reviews the methods by which the incubation period can be determined in these types of outbreaks. Other types of epidemics, such as those due to contact infection, those due to more than one cause, and pandemics are described. The courses followed by endemic infections are discussed, as well as the significance of these trends. The various diseases which have seasonal trends are described. There is some discussion on the evolution of newer " epidemics ", such as of leukaemia.

[This is a good descriptive review of epidemic curves, but there is little mention of any of the mathematical work on this subject.] *W. W. Holland*

World Health Organization. Technical Report Ser. No. 181. **Immunological and Haematological Surveys. Report of a Study Group. Geneva, 15–19 December 1958.** 35 pp. 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0·30; Sw. fr. 1.-.]

The epidemiology of infectious disease has been studied in recent years by means of surveys in both human and animal populations, in which serological tests are used for specific immunological reactions to a number of infective agents, particularly viruses. Examination of the blood can also yield information on the distribution of blood-groups, anaemias and haemoglobinopathies, and in biochemical nutritional surveys. This report by a WHO study group under the chairmanship of Dr. Frank Yates lists the conditions in the study of which blood examination has been useful, and those in which further research is necessary. Special sections are devoted to the uses and limitations of serological tests, to methods of sampling a population for such surveys, and to recommendations for the standardization of laboratory tests and of the methods of recording and reporting the results.

The Study Group suggest that, owing to the great number of possible tests which can be carried out on a single blood specimen, multi-purpose surveys should be undertaken where possible. They recommend the careful storage of sera in international collections administered by the WHO. These sera could be examined up to 20 years later, in the event of new laboratory techniques being developed for old diseases. Because of the great potential value of the stored specimens, the report recommends that continual efforts should be made to improve the methods of their collection and storage, and that their release should be carefully restricted by WHO, acting in consultation with experts in the proposed field of study. These proposals are considered suitable for adoption and implementation during the Public Health and Medical Research year proposed by the United Nations.

[This admirably clear and comprehensive summary should be read by those interested in this new and expanding field.] *A. S. Fairbairn*

MATERNAL AND CHILD HEALTH

Lean, T. H. **Maternal Mortality in Singapore—1955 to 1959.** *Singapore Med. J.* 1960, Sept., v. 1, No. 3, 87–95.

Maternal mortality in the State of Singapore has fallen from 7·6 per 1,000 births in 1930 to 0·52 in 1959. In the Kandang Kerbau hospital the rate was 1·0 per 1,000 births due to unbooked emergencies. The Malaysians had a maternal mortality about 10 times that of the Chinese and Indians, 4·1 per 1,000 compared with 0·49 and 0·59 respectively. Among the factors that adversely affected the Malaysian rate were their indifference to antenatal care and a disinclination for hospital confinements.

Age and parity were correlated with maternal mortality. 51·7% of the deaths were of women who had had 5 or more live births and 32·1% of the deaths were of women aged 36 and over. The principal causes of maternal mortality were toxaemia, 38·5%, haemorrhage, 27·9%, and medical conditions, 21·0%; about half of the medical conditions were heart diseases.

The author concludes that the maternal death rate could be considerably reduced by educating the women to accept antenatal treatment, by better co-ordination of the medical services, by better selection of women for hospital deliveries, especially older women and those in the high parity groups, by better liaison between physicians and obstetricians over problems of disease in pregnancy, and by the institution of an obstetric anaesthetic service. *W. J. Martin*

Gunther, Mavis, Aschaffenburg, R., Matthews, R. H., Parish, W. E. & Coombs, R. R. A. **The Level of Antibodies to the Proteins of Cow's Milk in the Serum of Normal Human Infants.** *Immunology.* Oxford. 1960, Oct., v. 3, No. 4, 296–306, 3 figs.

" The coated tanned red cell technique has been used to measure the level of serum antibody in normal infants to the proteins of cow's milk.

" In 286 sera of infants between the ages of 7 and 97 weeks titres up to 1000 were found with the mode around 64. This distribution was quite different from that found with adult and infant cord sera. Antibodies specific for casein, α-lactalbumin and bovine plasma albumin were shown to be present but none could be shown to β-lactoglobulin.

" The object of the study was to get evidence that some normal infants were sufficiently sensitized to cow's milk proteins to support the hypothesis that sudden ' cot death' in infants is due to an anaphylactic type of reaction consequent on inhalation of cow's milk."

PARISH, W. E., BARRETT, A. M. & COOMBS, R. R. A. **Inhalation of Cow's Milk by Sensitized Guinea Pigs in the Conscious and Anaesthetized State.** *Immunology*. Oxford. 1960, Oct., v. 3, No. 4, 307–24, 10 figs. [15 refs.]

"Introduction of 1 ml. of cow's milk proteins, in the soluble or insoluble form, into the respiratory tract of conscious normal guinea pigs produced negligible clinical effects. In animals sensitized to milk proteins similar treatment produced severe typical anaphylactic reactions and in some animals caused rapid death.

"In unsensitized guinea pigs, lightly anaesthetized to simulate sleep, similar administration of milk was without significant effect, but the inhalation of cow's milk by lightly anaesthetized sensitized guinea pigs resulted in an arrest of respiration and many of the animals died quietly without any struggle or excitement. The lungs of these animals did not show the acute emphysema characteristic of anaphylactic shock.

"The experimental results are presented in support of the hypothesis that 'cot death' in the human infant may be caused by a hypersensitivity reaction consequent on the inhalation of cow's milk proteins regurgitated from the stomach during sleep."

MCINTIRE, Matilda S. & SIMMONS, D. L. **Accidental Child Poisonings. Aspirin and other Medicines, not Household Chemical Specialties, are the most Commonly Ingested Substances in Accidental Poisonings.** *Soap*. New York. 1960, Sept., v. 36, No. 9, 99–101, 115–17.

Accidental poisoning in the young child is a growing problem. The first Poison Control Center established in the United States was in Chicago in 1953 [see PRESS, *J. Amer. Med. Ass.*, 1957, v. 163, 1330].

This paper contains an account of information obtained by a Poison Control Center opened in 1957 which became the master centre for the State of Nebraska. The centre is sponsored by the Children's Memorial Hospital where in 1957 356 and in 1958 529 cases of accidental poisoning in children were seen. The causes of these 529 cases were medicines (60·3%), pesticides (7·2%), agents for cleaning, polishing and "sanitizing" (13·6%) and others (18·9%). In 1958 visits by a public health nurse were made to investigate 423 cases of poisoning. The results, set out in tables, were: 77·5% cases were in the first 2 years of life and most of these were in the 1–2 year (31·4%) and 2–3 year (43·3%) groups. Boys were more frequently poisoned (57·7%) than girls. Aspirin was the most frequent cause (35%) among the medicines.

A number of other points were investigated such as the existence of accident proneness and various health problems which are described shortly. *M. E. Delafield*

LEITCH, I. & BOYNE, A. W. **Recent Change in the Height and Weight of Adolescents.** *Nutrition Abstracts & Reviews*. 1960, Oct., v. 30, No. 4, 1173–86, 2 figs. [20 refs.]

The heights and weights and the height-weight ratio of adolescents in three public schools, a physical training college and in two factories form the basis of the comparisons made in this paper. Maximum height is attained at an earlier age than formerly, particularly in the industrial groups. At the age of 15 there is no difference in physical measurements of the boys in public schools and in industry but the professional class grow more rapidly after this age and reach their maximum about two years earlier than the industrial group. Among adolescents weight has increased more than height in recent years. A comparison has also been made with some Scottish boarding schools and with the findings of some earlier workers. Danish recruits also show a spurt in growth and the reaching of maturity at a younger age than formerly.

W. J. Martin

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

FINNISH STUDENT HEALTH SERVICE [SAVONEN, K., Director]. **How it began and developed. How it works To-day.** 21 pp., 2 diagrams, 9 figs. and 4 graphs. 1959. Helsinki: Fabianinkatu 22, Finland.

Finland (population 4,400,000) has 4 college towns containing 13 different universities, colleges and other institutions of higher education. The total number of students enrolled is about 20,000; by far the largest student population is found in the capital Helsinki where there are 15,284.

The universities and colleges are non-residential. One-third of the students live at home, while two-thirds live in rented rooms (15% in student dormitories).

The student health service may be said to have started in 1932 when the Finnish National Anti-Tuberculosis Association began mass X-ray and tuberculin surveys of the students in Helsinki on a voluntary basis.

In 1946 the National Union of Students established the Student Health Service in Helsinki which included X-ray examinations of the chest, an outpatient clinic, medical staff, a students' infirmary, home visiting and care and health education. All this was paid for by the Union.

In 1954 the Student Health Foundation was established for the whole country with a centre in each of the 4 college towns. It is administered jointly by representatives of the State, the various institutions and the students and it receives State aid.

In 1947 and 1958 Acts of Parliament were passed obliging every enrolled student to be medically examined at stated intervals but so far the obligation only entails annual X-ray examination. The same Acts oblige students to pay a fee each semester for the Service.

The discovery rate of active tuberculosis was 8·7 per 1,000 in 1946 and 1·4 in 1958.

Student clinics have facilities for the reception, examination and treatment of patients. The physicians are full-time or part-time. Specialists are also available. Infirmary or hospital treatment is prescribed if needed, and students are visited when they are ill at home or in lodgings. The charge is about one-fifth of the regular fee. A nurse from the Centre also visits at need.

The Student Infirmary admits students with minor illness or if the housing conditions are poor. The only charge is for meals. Students admitted to hospital have the hospital bill paid by the Foundation for 6 months if the illness has begun during the academic year.

The Service has no sanatorium for tuberculous students, who are sent to their local sanatoria. Half the beds are free of charge in these sanatoria and if there is a charge the Foundation pays for 6 months. There is as yet no provision for the continuance of studies during the student's absence in a sanatorium but it is planned that this lack will be remedied.

The Student Dental Service was set up in 1955; it cannot yet meet all the demands made on it. The staff consists of full-time salaried dentists and nurses.

BCG vaccination of all new entrants was the rule until 1956 when it was confined to medical students and students in teachers' training colleges. In future BCG and polio vaccination will be compulsory for all students entering.

There is an active programme of health education.

H. G. Calwell

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

ANDREWS, J. D. B., INSLEY, M. L., ROGERS, W. F., SALKELD, G. & THOMAS, G. F. J. **The Problem of the " Young Chronic Sick ".** *Med Officer.* 1960, Oct. 28, v. 104, No. 18, 261–2.

This article defines the age range of the " young chronic sick " as 20–60 years.

The authors are geriatricians of adjoining hospitals in an area of South Wales containing a population of 1,100,000. The article excludes from consideration mental patients and epileptics, patients with only a few weeks to live and those suffering from arthritis or hemiplegia who are over 50 years of age.

In the area there are 1,041 geriatric beds in use, of which 83 were occupied by young chronic sick patients, and there were 12 awaiting admission. 61 of the 95 were men and 34 women; 19 suffered from disseminated sclerosis, 14 from hemiplegia and 10 from Parkinsonism; 9 were spastics and 9 had untreatable neoplasms.

In any scheme for their care the first essential is accurate diagnosis which is usually made in an " acute " bed. These illnesses are gradually progressive and the local authority, and the patient's relations, can generally make adequate arrangements for home care for a long period before admission to hospital becomes necessary.

Financial responsibility for institutional care may be taken by (a) Regional Hospital Boards, (b) Local Authorities, or (c) voluntary bodies. The work done by the " Cheshire Homes " is highly commended.

Regional Hospital Board provision may be by placing them with (a) young acute sick, (b) old chronic sick, (c) young handicapped, or (d) in separate establishments. On balance (d) appears to have the fewest disadvantages. For a population of 1,500,000 at least two 70-bed units or four of 35 to 40 beds each would be needed and the features required for success are set out.

[This small group of the sick usually receives scant attention.] *Allen Daley*

CHRONIC CARDIO-RESPIRATORY DISEASES

AMERICAN HEART ASS.: NAT. HEART INST. **Epidemiology of Cardiovascular Diseases Methodology Hypertension and Arteriosclerosis. Report of Conference, Princeton, New Jersey, April 24–26, 1959** [POLLACK, H., Chairman]. *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, Suppl., 1–124, illustrated. [Numerous refs.]

This supplement is the report of a conference which was held in Princeton, New Jersey, in April 1959 under the auspices of the American Heart Association, the National Heart Institute and the U.S. Public Health Service to consider methodological problems in population studies of cardiovascular disease—in particular, " hypertension and arteriosclerosis ". There were the following 4 major panels, for:

(a) Design and analysis of studies,
(b) Criteria for diagnosis of disease and clinical evaluation,
(c) Diet, physical activity and biochemical measurements,
(d) Cultural, society, familial, psychological and genetic influences;

panels (b) and (c) were divided into 4 and 3 subcommittees respectively. The participants were all resident in North America, but the majority are well known on this side of the Atlantic.

In his opening remarks Dr. Herbert POLLACK (pp. 6–8), the chairman, told the conference that it had 3 primary aims: (1) to set up a minimum baseline, and thus to provide a basis for comparability in epidemiological surveys; (2) to suggest optimum procedures; and (3) to suggest studies which would fill existing methodological gaps. The first three panels and their constituent sub-committees carried out this briefing, some brilliantly, some adequately. The group which considered culture, society and genetics, failed however—a fact which, to judge from a comment in the preface, was realized by the editor, if not by the group itself.

The majority of the sections of the supplement are brief and incisive; when there have been other committee reports on the topics under discussion published by organizations such as WHO, the American Heart Association, etc., these are mentioned, and are either recommended or rejected with good reasons given. In most sections full cognizance is taken of work which is being done outside the United States. The statement from the fourth panel is very long, and is studded with words unfamiliar except to the sociologist such as "areal" and "antithetical", "societal" and "ideational"; much of it is interesting, if not entirely to the point, and some of it highly controversial. Such recommendations as are made however are inclined to get lost among the pages of diffuse theory.

There are some minor general criticisms. There seems to have been a lack of cross-checking of manuscripts; for instance, although the sub-committee on physical activity correctly emphasizes that the ponderal index, though useful, cannot distinguish the obese physique from the muscular, this index is spoken of as "an index of fatness" by the panel on experimental design. Again there is a tendency throughout the supplement to equate atherosclerosis exactly with coronary heart disease, and therefore to overlook the importance of the whole question of clot formation; the epidemiology of hypertension is also often pushed into the background.

The penultimate chapter reviews the epidemiological surveys in cardiovascular disease presently under way in the United States. Many of these have not yet been published and include such interesting projects as long-term research on Navajo Indians living in their reservation in Arizona, and on the monks in two monasteries—one of which is a closed community.

All those engaged in this general field should read this report. In particular workers contemplating new surveys should give the recommendations—especially those on diagnostic criteria and standardization of laboratory techniques—their most careful consideration, for here at last is a potential means of making valid comparisons between one population study and another.

Roy M. Acheson

CANCER

DUNN, J. E., Jr., LINDEN, G. & BRESLOW, L. **Lung Cancer Mortality Experience of Men in Certain Occupations in California.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1475–87. [10 refs.]

In a previous study [BRESLOW *et al.*, this *Bulletin*, 1954, v. 29, 623] data obtained about the past occupational histories of patients with and without lung cancer suggested that there might be a high risk of lung cancer among certain occupations in California. The numbers of cases in the various groups were, however, small and in only one was the excess of lung cancer statistically significant. In the present study questionnaires were sent to men in 10 occupations, one of which served as a control. Questions were asked about occupation and smoking habits. Replies were received from approximately 65,000 men—85% of those written to.

The mortality among these men over the next 3–4 years from (i) lung cancer and (ii) all cancer other than lung cancer was obtained by comparing their names with the death entries recorded in the State. Cases will have been lost if the men left the State during the follow-up period; but the loss is unlikely to have been more than 2% per year. The mortality will also have been under-estimated as a result of ignoring the reduction in the number of man-years at risk due to total mortality. This error is small and produced an over-estimate of approximately 2% in the population at risk for the entire period studied.

The expected mortality from cancer other than lung cancer was obtained from the age-specific death rates in California at the time of the 1950 census and the number of man-years at risk at each age in each of the occupational groups. The expected numbers of lung cancer deaths were estimated similarly, save that the lung cancer mortality in California was assumed to have increased between 1950 and 1956 at the same rate as lung cancer had increased throughout the United States.

The results showed that the total mortality from cancer other than lung cancer was 85% of the expected and ranged from 67% to 133% for various occupational groups. For lung cancer the total mortality was 113% of that expected, ranging from 26% in printers to 145% in painters. The control occupation gave a figure of 86%. Some of the excess lung cancer mortality could be attributed to the fact that men in some of the occupations smoked more than men in the control group, whereas men in the control group had smoking habits similar to those recorded in other samples of the Californian population. Since the mortality from lung cancer was 29 times as high among men smoking two packets of cigarettes a day as among men not smoking cigarettes, smoking had to be taken into account. Another adjustment was also required to take account of the cases missed. On the assumption that there was no major occupational risk from cancer other than lung cancer this could be done from the under-estimate of the mortality from this cause. After these corrections had been made, the ratios of observed to expected mortality were: control group 1·01 : 1, cooks 1·66 : 1, painters 1·48 : 1, asbestos workers 1·41 : 1, marine engineers 1·30 : 1, plumbers 1·27 : 1, welders

1·14:1, sheet metal workers 0·63:1 and printers 0·25:1. The excess was statistically significant for cooks and painters.

In view of the large risk associated with cigarette smoking, it is difficult to obtain evidence for anything other than a large occupational risk. It is estimated, for example, that for the observed mortality to be double the expected mortality it would be necessary for the mortality among non-smokers to be increased more than 8-fold. Doubling the mortality among non-smokers would lead to an increase in general mortality of only 14%.

Richard Doll

PAYNE, W. W. & HUEPER, W. C. **The Carcinogenic Effects of Single and Repeated Doses of 3,4-Benzpyrene.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 350–55, 6 figs.

Low level, long-term exposure to carcinogens may be encountered more often in practice than a single exposure to a large dose. It is, therefore, important to study the carcinogenic effect of material applied in this way as well as to demonstrate the effect of single doses. In the present study, a comparison has been made between the carcinogenic effect of 3,4-benzpyrene injected subcutaneously into the neck of a mouse (1) in a single dose, and (2) in 12 split doses given at monthly intervals. Groups of 36 male and 36 female mice were used to study the effect of each dose schedule. No tumours were obtained in control animals injected with the solvent alone. No tumours occurred in mice given doses of 0·008 or 0·013 mgm. Mice given 0·025 mgm. showed tumours in 10% of animals when the dose was injected at one time and in 3% of animals when it was split. Corresponding figures for larger doses were: 0·05 mgm.—10% and 10%; 0·1 mgm.—24% and 38%; 0·25 mgm.—28% and 61%; 0·5 mgm.—25% and 74%. In each case the average latent period was decreased with increase of dose and was longer when the dose was split than with a single injection. It is notable that an average of approximately 25% incidence was reached with a single dose of 0·1 mgm. or more, but that the proportion of affected animals continued to rise when larger doses were given at monthly intervals.

It is concluded that a given amount of carcinogen is more effective for mice when administered in small increments over a long period of time than when administered in a single dose. It may be, therefore, that low level, recurring exposure to a carcinogen is more hazardous than single exposure to the same total amount.

Richard Doll

STABERG, Else M. Tjär- och nikotinmängden i cigarrettrök. En jämförande undersökning av olika cigarrettmärken samt studier över effekten av röklängd och röksätt. **[Content of Tar and Nicotine in Cigarette Smoke. Comparisons between different Cigarette Brands and Studies of the Effect of Duration and Mode of Smoking]** *Nordisk Hyg. Tidskr.* 1960, v. 41, Nos. 9/10, 199–216, 8 figs.

The English summary appended to the paper is as follows:—

"The content of tar and nicotine in smoke from regular, kingsize and filter cigarettes was estimated. Twenty-nine brands were studied, 15 of them Swedish.

"The influence on tar and nicotine content of the length of cigarette that has been smoked, puff volume, puff duration and puff interval was also studied."

[The original should be consulted for details.]

See also p. 236, BÖHME. **[Asbestosis and Cancer of the Lung. Parts I and II.]**

See also p. 235, WAGNER, SLEGGS & MARCHAND. **Diffuse Pleural Mesothelioma and Asbestos Exposure in the North Western Cape Province.**

MISCELLANEOUS DISEASES

PELTOLA, P. Strumaendemiens etiologi i Finland. **[The Aetiology of Endemic Goitre in Finland]** *Nordisk Med.* 1960, Dec. 1, v. 64, No. 48, 1511–12. [31 refs.]

The English summary appended to the paper is as follows:—

"Conflicting results have been obtained in studies of the etiology of endemic goitre in Finland, based on dietary iodine intake or on iodine excretion. A summary is given of the investigations performed by the writer and his co-workers, which suggest the presence of a goitrogenic factor of the thiouracil type in cow's milk. These investigations, as well as the nature of the endemic goitre in Finland, support the possibility that this goitrogenic factor may play a decisive role in the causation of endemic goitre in Finland, especially as iodine deficiency could not be definitely demonstrated in the areas concerned."

INTERNAT. DIGEST HEALTH LEGISLATION. 1960, v. 11, No. 3, 387–98. [18 refs.] **Endemic Goitre. Legislation on Iodine Prophylaxis.**

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

MEYER, R. Auswertung zweigipfliger Überlebenskurven der *Salmonella paratyphi* B im Grundwasser. **[Double Peaks in the Survival Curves of *Salmonella paratyphi* B in Ground Water]** *Arch. f. Hyg. u. Bakt.* 1960, Oct., v. 144, No. 7, 564–8, 1 fig.

In previous work the author has described the presence of bactericidal agents in certain ground waters of the East Frisian area. The present paper contains an account of experiments on the survival of *Salmonella paratyphi B* in these ground waters with a description of the statistical procedure adopted to assess the significance of the findings. The main result of the experiments was to show that the bacterial numbers after inoculation of the water did not decrease regularly but showed an actual increase within 40 minutes followed by a fall, and again after 7 hours a considerable increase which continued to a maximum on about the second to the fourth day before the final continuing decrease in numbers.

The suggestion made by the author is that these changes may be due to alternating adsorption of the bactericidal agents by iron oxides contained in the water and their subsequent elution. *M. E. Delafield*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

ISAAC, P. C. G. [Editor.] **Report on Research carried out by the Public Health Engineering Section in the Year ended 30 June 1960.** *Univ. Durham, King's College, Dept. Civil Engineering, Bull. No. 21.* 1960, Oct., 24 pp., 9 figs.

This Annual Report for the year ended June 30, 1960 of the activities of the Public Health Engineering Section of the Department of Civil Engineering of the University of Durham contains accounts of researches carried out, records of measurements of atmospheric pollution and a list of publications during the year.

Work on the biological oxidation of synthetic detergents has continued and the respiration of the organisms of settled sewage in the presence of "sucrose monostearate" (Herstein) and sodium Dobane JN sulphonate has been studied manometrically.

The vertical distribution of bacteria in trickling filters was studied by means of an experimental filter described in last year's report [this *Bulletin*, 1960, v. 35, 535]. This filter (of which a photograph is given) has been brought into full-time operation after certain difficulties and drawbacks had been overcome. The preliminary results of bacterial counts are given in figures which illustrate diagrammatically the percentage distribution of film at different times of the year throughout the sectional filter.

There is a description of the design and construction of a 4-unit pilot-scale trickling filter plant in the sewage works in the Urban District of Felling.

A brief investigation was made on the occurrence of *Salmonella* spp. in the sewers of Newcastle. 6 sets of samples were taken from 7 main sewers. From 2 samples cultures were isolated that appeared to resemble *Salmonella* spp. 1 of these cultures died but the other was confirmed as *Salmonella paratyphi A*. *M. E. Delafield*

ATMOSPHERIC POLLUTION

NATIONAL SOCIETY FOR CLEAN AIR. **The Proceedings of the Diamond Jubilee International Clean Air Conference, London, 20–23 October 1959.** 284 pp., illustrated. 1960. London: Field House, Breams Buildings, E.C.4. [30s.]

The conference concerned attracted delegates from all parts of the world where air pollution has been considered seriously, and the 78 papers are extremely varied in every way. Some are of considerable interest, but they are directed at a completely lay general public and are unlikely to be of use to anyone seriously concerned with the problem. *John McK. Ellison*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

VIGLIANI, E. C. L'insegnamento della medicina del lavoro nell'Europa Occidentale. **[The Teaching of Industrial Medicine in Western Europe]** *Med. d. Lavoro.* 1960, June–July, v. 51, Nos. 6/7, 415–26.

Professor Vigliani of Milan briefly reviews in his paper what graduate and postgraduate teaching of industrial medicine and hygiene, and occupational health, is available in each of 17 Western European countries. He is not quite accurate in what he says about the position in the British Isles: he states, for instance, that the D.I.H. is awarded in London by the Royal Institute of Public Health and Hygiene and by the Society of Apothecaries, and that Irish students have to come to Britain for their D.P.H. as well as for their D.I.H.

Bernardino RIMAZZINI taught clinical medicine in Modena and Padua over 250 years ago and he was the "founder" of industrial medicine. DEVOTO of Pavia began teaching the subject again at the beginning of this century, and he opened the Clinica del Lavoro at Milan in 1910. 11 Italian universities now provide specialized teaching in this subject at postgraduate and 8 at graduate levels: refresher courses are also available. The relative special diploma is not yet compulsory for those who practise insurance and factory medicine. Occupational medicine in Italy has had its beginnings in clinical medicine.

In France, it was the practitioners of forensic medicine who first interested themselves in the subject, and a close association of occupational with forensic medicine persists in a number of French universities, where both graduate and postgraduate instruction is provided. The *certificat d'études spéciales* in occupational medicine is now required by all those who have to apply this speciality in their practice; and every firm or other undertaking which employs over 50 persons must have its medical officer.

The orthopaedic surgeons in Spain were responsible for developing occupational medicine, following up their experience of casualty work and the study of accidents and of how to prevent them.

Holland requires every medical student to sit an examination in social, which includes occupational, medicine. The University of Leyden holds postgraduate courses in public health and preventive medicine and these include a 5-months' course in occupational medicine.

Yugoslavia follows British and U.S. practice and associates the teaching of industrial medicine with that of public health and hygiene.

Switzerland has the unique provision of a chair and institute for the teaching of the physiology and hygiene of labour at its Federal Polytechnic: engineers who wish to specialize in the "production sciences" take, in addition, a course on "Human Labour", which is applied psychology.

Among the Scandinavian countries, Finland provides a postgraduate course in occupational medicine, which takes 3 years, at a special Institute in Helsinki.

J. Cauchi

VIGLIANI, E. C. & PARMEGGIANI, L. L'evoluzione della patologia professionale in rapporto al progresso tecnologico. **[The Evolution of Occupational Disease as Compared with Technical Progress]** *Med. d. Lavoro.* 1960, Aug.–Sept., v. 51, Nos. 8/9, 503–17.

This is an extensive review of the position from the early years of this century to the present time. The authors point out that the statistical bases of comparison have had to be changed frequently in view of the progress of industrial medicine, because of alterations in the compensation status of diseases and of the introduction of new diseases into the schedules. These points are illustrated by reference to a number of conditions such as poisoning by lead, phosphorus or mercury, ankylostomiasis, vesical lesions due to aniline compounds, silicosis, occupational dermatitis, noise deafness, certain more recent causes of risk like beryllium and boron and their compounds, plastics, insecticides, atmospheric conditions, and finally the problem of mental health in relation to mechanization and automation in industry.

Dealing with lead poisoning, the authors state that nowadays persons working with accumulators and ceramic painting are those most exposed to risk; mercury poisoning was especially frequent in the immediate post-war (1939–45) period but the change in men's habits of now going without a hat has greatly reduced the number of cases arising in the felt-hat industry; ankylostomiasis, except for the sulphur mines in Sicily, now affects only agricultural workers and their families.

The pneumoconioses now make up 85% of all the occupational diseases for which compensation is payable for permanent injury or death. From 1956 an important change in the law reduced the level of invalidism for which compensation is payable from 33% to 21%. The uncomplicated disease shows a progressive increase in the number of patients receiving permanent compensation, but since preventive measures are now very extensive and detailed this shows rather that there is an increase in the number of workers exposed to risk and also more accurate diagnosis; silico-tuberculosis on the other hand shows a definite diminishing tendency due to annual X-ray examinations and early detection of those exposed to risk and the use of specific drugs.

Compensation for occupational dermatitis only started in Italy in 1953. The present reported incidence is very low, which may possibly be due to the darker skins of Italians when compared with Anglo-Saxons, but the figures are not really reliable.

In regard to noise deafness it has been found that prolonged exposure to 85–90 db for months or years can cause irreversible injury, especially in the higher tones (3000–4000Hz). Noise also aggravates tiredness in the worker, especially if it is discontinuous, varied and sudden.

Present Italian law does not include boron and its compounds, *e.g.* the boranes, among the substances likely to cause occupational disease. For plastics, the epoxy resins and polyurethanes can have a sensitizing action on the skin or cause asthmatic attacks; the former may have a possible carcinogenic action also.

Regarding atmospheric contamination, the authors say that in the winter in Milan the number of particles per cc. can reach 2000, 50% of which are less than 0·6μ in diameter.

The atomic industry is so well controlled that practically no case of a compensatable *disease* resulting from radioactive materials has been reported, only accidents.

The ever increasing rhythm, acceleration of work schedules, time and motion study and so on, make considerable demands on the worker's psychological make-up, and changes from the traditional methods to mechanization and now automation are rapid rather than gradual. There is a sympathetic appreciation of the position of workers in a large factory just doing one rather monotonous job who may well feel that they are only units instead of people.

Summing up, the authors point out that over the years very considerable improvements have taken place; a great deal remains to be done such as substitution of lesser for more toxic materials, *e.g.* toluol for benzol, while the importance of adhering strictly to the maximum allowable concentration laid down is fundamental. Looking to the future they consider that there may well be an increase in the neuroses of salaried workers while the use of new forms of high energy may extend the risks of chronic poisoning. The coming automation may lead to a change in the manifestations of occupational diseases. As a result preventive measures must be directed not only to the worker's physical fitness but also to his psychology and to improvements in his expertise.

[The status of the authors, especially the senior author, is so high in the world of industrial medicine that it is rather surprising, particularly in view of the considerable Italian textile industry, to find no mention of byssinosis—presumably therefore it does not occur in Italy—and very little about asbestosis though according to Battigelli (this *Bulletin*, 1960, v. 35, 432) a relatively high proportion of the workers in this industry are suffering from the disease. A point might well have been made of the silicosis affecting workers in abrasives; here occupational disease has certainly kept pace with modern technological processes (see Battigelli *loc. cit.*).] *W. K. Dunscombe*

Trans. Ass. Indust. Med. Officers. 1960, Oct., v. 10, No. 3, 80–84. **The Medical Branch of the Factory Inspectorate of the Ministry of Labour. Summary of four papers given at a meeting of the Association on 25th March, 1960.**

These papers are designed to give an indication of the variety of duties carried out by H.M. Medical Inspectors of Factories. R. Owen, a divisional medical officer, in his work, has the same powers as the lay inspectors but he can also carry out such medical examinations as are necessary for the purposes of his duties. He advises the lay inspectorate on the medical aspects of their work. The advice of divisional medical officers is sought in connexion with newly appointed Medical Officers, with whom he has to co-operate. The wide questions relating to first aid services are also referred to him.

S. G. Rainsford is in charge of the Medical Laboratory Service which came into existence in 1959. This service is still in the experimental stage, and is planned to undertake, among other things, work of a clinical pathological nature. Most of the work undertaken has been concerned with conditions likely to give rise to industrial disease, and mention is made of the complete haematological investigation in workers exposed to the hazards of ionizing radiations. An example of the work is that of the investigation of 300 workers exposed to a lead risk, to determine the value of aids to diagnosis.

It was considered that the haemoglobin level in the blood and the amount of coproporphyrin in the urine provided the most valuable information.

A. T. Doig reviews the advances made during his 21 years with the Factory Inspectorate. The improvements in the incidence and mortality of notifiable diseases such as lead poisoning, toxic jaundice, epitheliomatous ulceration and mule-spinners' cancer are detailed. Bladder cancer and dust diseases have been amply investigated.

The medical inspectors have also been closely associated with the development and improvement of apparatus for suppressing and removing dust and for assessing airborne concentration of dust. Doig pays tribute to the contributions of medical inspectors to the advance of medical knowledge and mentions particularly, Legge, Collis, Middleton, Henry, Merewether, McLaughlin and Browning.

S. Horner tells of the increase in numbers of medical inspectors in 36 years from 5 to 19. This increase gives the inspectors a greater opportunity to study in detail as many as possible of the influences which affect industrial health. They are able to discuss problems in the field of industrial health with medical officers of firms. The role of the Appointed Factory Doctor is the carrying out of statutory examinations and this provides material for the review of preventive measures.

Close relations are maintained with doctors of the Health Service and with other government departments including the Ministry of Pensions and National Insurance. Panels of experts in dermatology, ophthalmology and radiological matters have been set up to study and give advice on these three subjects.

Charles L. Sutherland

Ministry of Labour and National Service. **Annual Report of the Chief Inspector of Factories for the Year 1959** [McCullough, T. W.]. Cmnd. 1107. 128 pp., 1 diagram. 1960. London: H.M. Stationery Office. [7s.] [Refs. in footnotes.]

The number of reported accidents increased from 167,697 in 1958 to 174,071 in 1959. This disappointing reversal of the earlier downward trend occurred in spite of increased efforts on the part of the accident prevention movement. The level of industrial production increased considerably during 1959, and the increased number of accidents may

be partly explained by increases in the numbers of people employed and hours worked. The number of fatal accidents fell from 665 in 1958 to 598 in 1959. The latter figure represents the lowest number of fatal accidents reported in any year during the present century.

The number of accidents to young persons increased from 9,838 in 1958 to 11,001 in 1959, and this was not due to an increase in the numbers employed.

In the present Report changes have been made in the analysis and classification of information about reported accidents. In addition to tables analysing accidents by industry, causation and process, there is included for the first time a table giving accident incidence rates for the majority of industries. Those rates show the numbers of accidents per 1,000 workers subject to the Factories Acts. In the future, yearly changes in these rates will indicate any real changes in the incidence of accidents in the various industries.

It is evident from the large number of accidents to the head and neck, to the eyes, to the feet and ankles, and to the hands, that much could be done to reduce them by the wearing of suitable protective clothing.

Some industrial developments which have a bearing on safety, health and welfare are reviewed. Fire and explosion on petroleum premises may be caused by faults in electrical equipment. Examples are given of explosions caused (a) by a thermostat switch that was not flameproof, and (b) by a small leakage of current on a lighting fitting on a petrol pump, which latter risk could have been avoided by the use of suitable earth-leakage protective equipment such as is available nowadays.

An electrical method which provides a solution to the problem of explosions in large ammonia-compressor houses has now been worked out. Developments in electronic and semi-conductor engineering which have an effect on industrial safety are mentioned.

Among engineering developments which affect safety are (a) the use of disc brakes on two-roll mills in rubber works; (b) the introduction into the clothing industry of mechanically-driven power presses of the positive clutch type; (c) the use of hydraulic power for leather machinery, and (d) the increasing use of automatic-feed mechanisms instead of hand-feed mechanisms in the printing industry.

In non-ferrous foundries an efficient method of controlling the fumes from crucibles of molten metal has recently been developed, and a new type of reverberatory furnace has been introduced which dissipates considerably less heat, and thus improves the working environment.

Promising results have been obtained in iron foundries by the drying of ladles by electricity or gas, so as to obtain more efficient drying and reduce fume.

In steel foundries two hot-fettling processes have been introduced in order to minimize the production of dust containing free silica. Both methods give rise to hot fumes which should not be allowed to disperse into the general atmosphere, but the generation of free silica is avoided.

To guard against rust in various industries the practice of giving a protective application to the internal surfaces of hollow vessels is becoming more frequent. Such protective coating involves the use of preparations containing toxic solvents, which can be harmful to workers in a confined space. The provisions of Sect. 6 of the Factories Act, 1959, apply to work of this kind.

When ammonium nitrate is used in the manufacture of silica bricks of low porosity risks arise from the ammonia evolved during grinding, and from oxygen, nitrogen tetroxide and nitric oxide which are given off during firing. The methods of guarding against these risks are outlined.

Reference is made to the safety problems of construction, and of maintenance and repair, which arise in connexion with buildings up to 400 ft. in height, such as are now being built in various parts of Britain.

In a chapter on designing machinery for safe operation emphasis is laid on the need for a realization at the earliest stage of the dangers that may arise, so that foolproof safeguards can be built in.

Reference has already been made to the increased number of accidents to young persons. A special chapter is devoted to a discussion of the prevention of accidents to young persons.

Detailed accident statistics are given in the 24 appendices to the Report. [For 1958 Report, see this *Bulletin*, 1960, v. 35, 13.] *Thomas Bedford*

MINISTRY OF LABOUR. **Annual Report of the Chief Inspector of Factories on Industrial Health 1959** [McCULLOUGH, T. W.]. Cmnd. 1137. pp. iii + 60. 1960. London: H.M. Stationery Office. [3s. 6d.]

The Factories Act, 1959, lays upon the Minister a new duty to promote health, safety and welfare in places subject to the Factories Acts by collecting and disseminating information, and by investigating and helping to investigate problems in this field. The Minister is also empowered to provide and maintain laboratories and other appropriate services for such investigations. Other provisions clarify and slightly extend the Government's powers to control the use of dangerous materials, appliances or processes in factories, and to prohibit the importation of dangerous materials and articles. The Act of 1937 prohibited the employment of young persons to lift excessive weights, and the new Act extends this provision to any person of any age.

The First-aid Boxes in Factories Order, 1959, revised the requirements for first-aid boxes. All antiseptics are now omitted, sterilized dressings are to be unmedicated, and an approved eye ointment replaces cocaine eye drops. The provision of adhesive wound dressings is now obligatory.

During the year the report of a committee on anthrax was published. The number of cases of anthrax has dropped significantly, especially in recent years, and even more significant has been the decline in the number of cases ending fatally. The decline of cases has not been spread evenly over the industries using materials that carry the risk of anthrax. Since the war the disease has increased in industries handling bones and bone meal; and half the number of fatal external cases that have occurred recently were attributable to these materials. The Committee made recommendations about the control of imports and the compulsory disinfection of some materials, precautions to be taken in factories, and improved arrangements for early diagnosis and treatment.

There were notified 64 cases of lead poisoning, an increase of 9 on the 1958 figure. No case was fatal. 2 cases were reported from a plant in a metal refinery where

lead and tin dross were reduced in an oil-fired furnace, and it was thought that the poisoning might have been caused by dust from the dross. Among oxy-acetylene burners employed in ship-breaking yards there were 15 cases, as compared with an average of 9 in the previous 5 years. It appeared that, in general, the burners were reluctant to wear the respirators provided, and preferred to take other precautions such as standing to windward of the material being cut. Some of those affected had been so employed for relatively short periods, and were thought to be less adept than their fellows in avoiding fumes. Of 14 cases classed as "Other contact with molten lead", 5 occurred within a short period in the same factory. 3 of the men were overhead crane drivers, 1 was a furnace man, and the other had been employed on furnace repairs.

There were 2 cases of mercurial poisoning, 1 of arsenical poisoning, and 25 of aniline poisoning. No case of chronic benzene poisoning was reported. 16 reported cases of compressed-air illness were confirmed, but with 1 exception all those affected showed only slight signs and symptoms of the "bends", and recovered rapidly when recompressed; the other case was severe and showed evidence of cerebral involvement.

There were 6 cases of anthrax, one of which was fatal. In the patient who died the source of infection was not identified, of the others wool was the source of infection in one instance, and in the other 4 hides and skins were responsible.

The total of 192 cases of chrome ulceration was rather lower than the average number reported in recent years. 100 cases occurred in factories manufacturing chromates and bichromates, and only 10 of those affected had to stay from work. 85 cases occurred in the processes of chrome plating and anodizing, and in 35% of these there was nasal ulceration. Regulations require the provision of efficient exhaust draught at plating baths, but exemption may be given where an approved spray-suppressing compound is used on the surface of the chromium-plating bath. But the suppressing compound is not always effective. At one works at which a method for producing "crack-free" chrome is used, with the bath operated at a higher temperature than usual, spray-suppressing material was used in place of local exhaust ventilation, but 6 men were found to have nasal ulceration. The employment of young persons at a chromium-plating bath is prohibited, but it is not always understood that by definition this prohibition applies also to a swilling bath for articles after plating. 7 young persons were found to have ulceration, including a boy of 15 who had nasal ulceration. 3 other cases of nasal ulceration occurred among workers with a hot chromate solution. A woman sweeper in a plant making green oxide of chrome containing some bichromate impurity developed bilateral nasal ulceration.

There was a total of 226 cases of epitheliomatous ulceration, 190 of which were attributed to pitch or tar. Of these 190 cases 124 were described as a wart or warts.

The numbers of deaths from fibrosis of the lungs, including all forms of pneumoconiosis and byssinosis, as notified to the Registrar-General, are tabulated.

The report ends with an instructive chapter on dusts and their effects on the lungs. [For 1958 Report, see this *Bulletin*, 1960, v. 35, 14.] *Thomas Bedford*

MILLIKEN, T. W. & WESTON, T. S. **Grease Gun Injuries.** *New Zealand Med. J.* 1960, Sept., v. 59, No. 337, 413–16, 8 figs.

"Over the last few years, several cases of injuries involving the injection of grease and oil into the tissues have been described." This paper records 2 cases of grease gun injury in the first of which a mechanic had just injected grease at a pressure of about 3,000 lb. per square inch into the pulp of the left index finger. On examination there was only a small puncture wound distal to the terminal joint and no pain. Local evacuation of grease by incision was performed but in spite of prophylactic incision the finger after some days became septic. 2 weeks after the injury the finger was opened from the distal end to as far as the base of the web. Grease was found to have infiltrated the subcutaneous tissue from the pulp to near the web. Later the finger had to be amputated. The man returned to work after 3 months.

In the second case a garage attendant had accidentally brushed his forehead with the nozzle of the grease gun 2 weeks previously. He had a tender swelling above the right eyebrow from which a small fibrous mass with a small central cavity containing grease was removed by operation and was found to have the histological appearance of a grease granuloma. He made a rapid recovery. There are some very good photographs to illustrate these cases.

In the discussion there is reference to the prophylactic recommendations which may not be carried out by the grease gun user. In the first case, for example, the mechanic had removed the guard round the needle point of the gun. From the clinical point of view:—"It is questionable whether the final outcome of our first patient might have been more satisfactory if more radical surgery had been carried out earlier, but the deceptive paucity of the symptoms at the outset persuaded against this". Stress is laid on the point that the initial injury may appear trivial although the actual tissue involvement may be great. *M. E. Delafield*

GOLDING, F. C., GRIFFITHS, P., HEMPLEMAN, H. V., PATON, W. D. M. & WALDER, D. N. **Decompression Sickness during Construction of the Dartford Tunnel.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 167–80, 7 figs.

This paper describes a clinical, radiological and statistical survey of decompression sickness which was carried out during the construction of the Dartford Tunnel between Kent and Essex. Over a period of 2 years, 1,200 men worked eight-hour shifts in compressed air on this project, with between 250 and 320 on the active list at any one time. This involved 122,000 compressions of which 119,000 were at pressures over 16 pounds per square inch (p.s.i.) and up to 28 p.s.i. There were 685 cases of decompression sickness, 650 of which were classified as Type 1, or simply "bends" and 35 as Type 2, more serious and more complicated. In Type 1 patients, the complaint was one of pain, usually described as being in or around a joint. In 85% the lower limbs only were affected; in 7% upper limbs only; in 8% both upper and lower limbs. Pain started on the average about three hours after decompression, but the time of onset varied

considerably, from immediately after decompression to 12 hours later. Type 2 cases always start early and the average time of onset was approximately 50 minutes after decompression. A summary of the presenting signs and symptoms in Type 2 patients is as follows: 26 with vertigo, 15 with signs of "shock", 6 with visual symptoms, 5 with paralysis of limbs, 5 with epigastric pain, 4 with dyspnoea, 3 with speech defects, 1 with epileptiform attack, 1 with signs suggesting a cardiac lesion, and 1 who collapsed and was unconscious on leaving the decompression lock. The average age of Type 1 patients was 30 years and of Type 2 patients, 36 years. In general Type 2 patients reacted to therapeutic recompression more dramatically than did Type 1 patients; improvement usually began at comparatively low pressures, often considerably below working pressure. 22 men showed extensive skin "mottling" after decompression, 15 being obese, and as some authorities consider this occurrence to be of serious prognostic significance, they were either forbidden to work in compressed air, or limited as to time and pressure. 45 men exposed to pressures of less than 18 p.s.i. developed decompression sickness, 41 being Type 1, and the remaining 4 Type 2.

A preliminary radiological survey of bone damage in compressed air work was started and included men who had suffered an attack of bends and some who had only minor symptoms or mottling of the sin. It was discovered that aseptic necrosis may be found in the absence of a history of bends for which treatment has been sought and in persons who have worked for years in compressed air and are still working without symptoms. During this survey 2 serious cases were discovered to have cysts in the lungs and it is suggested that these gave rise to air embolism when the subjects were decompressed. It is also suggested that pulmonary changes may contribute more than hitherto believed to the pathogenesis of bends.

Men vary in their susceptibility to bends and a relatively small group of persons was responsible for quite a large proportion of the attacks. The existence of acclimatization to pressure was confirmed; it is such that the bends rate may fall in two to three weeks to 0·1% of the incidence on the first day of exposure. Acclimatization is lost again, with a "half-time" of about 7 days, if a man is away from work. The existence of processes of acclimatization and "de-acclimatization" seems to account for a great deal of the apparent randomness in the attacks of bends. It was found that working at low pressures for a few days does not appear to confer any measurable benefit on men subsequently introduced to higher pressures. If acclimatization could be deliberately induced, without harm, and retained, this alone could lower the bends rate by a large factor; but no means of doing this can yet be indicated.

During the construction of the tunnel, the decompression tables recently prescribed by the Ministry of Labour were used but evidence was obtained that they could be made safer and it is recommended that tables based on 15 p.s.i. and 8-hour saturation be tested. In the authors' experience the treatment of decompression sickness is best accomplished by keeping the therapeutic pressure as low as possible, so as to minimize any contribution which absorption of nitrogen during the recompression itself may make to recurrence of the lesion. All cases in this contract were successfully treated and no fatality or permanent disability occurred. [This is an extremely interesting publication containing much information and discussion of great interest and it is recommended that it should be read in the original.] *P. J. R. Challen*

GRIBBLE, M. de G. **A Comparison of the "High-Altitude" and "High-Pressure" Syndromes of Decompression Sickness.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 181–6. [Numerous refs.]

Decompression sickness at low pressures was first described by VON SCHRÖTTER in 1906. He exposed himself to an atmosphere of 230 mm. Hg (29,500 ft.) and noticed joint pains. The first authentic case of high-altitude decompression sickness was not recognized, however, until 1938 (BOOTHBY and LOVELACE, *J. Aviat. Med.*, 1938, v. 9, 172), though it rapidly became recognized as an entity with the great increase in high-altitude flying during the second world war. This paper, based on published descriptions and personal observation, gives an account of subjects exposed to low pressures in a partially exhausted "decompression chamber" rather than in aircraft. Under these conditions high-altitude decompression sickness is never seen below 23,000 ft. (307 mm. Hg), and extremely rarely below 30,000 ft. (225 mm.), but it occurs increasingly frequently at greater altitudes (GRAY and MASLAND, *ibid.*, 1946, v. 17, 483). The most common symptom is joint pain, but other complaints are itching of the skin, faintness, chest pain known as "chokes", dyspnoea with a feeling of suffocation and apprehension, and neurological phenomena. Paralysis is extremely rare and is found as commonly in the arm as in the leg. A common symptom is homonymous scintillating scotomata and these, like chokes, may persist for up to an hour after recompression but are never permanent. The most serious manifestation is post-decompression shock, which, although very rare, may be fatal. Clinical evidence of shock nearly always appears after recompression is complete, and may be delayed for as long as eight hours. In one million man-exposures to 30,000 ft. and above there were about 150 serious cases of post-decompression shock (0·015%) of which 7 were fatal (ADLER, U.S.A.F., S.A.M., *Project Report,* Randolf, A.F.B., Texas, 1950). The main necropsy findings in high-altitude post-decompression shock have been pleural and pericardial effusions, oedema of the lungs, acute dilatation of the heart, congestion and oedema of the brain, and a fatty liver.

Mild cases of the two syndromes are very similar but severe cases differ significantly. Persistent paraplegia, aseptic bone necrosis, and death due to gross air embolism are characteristics of high-pressure decompression sickness, whereas post-decompression shock is very much commoner after exposure to altitude. Degenerative changes in the central nervous system occur in both syndromes but are found mainly in the grey matter of the cord after exposure to pressure, and in the white matter of the brain in high-altitude decompression sickness.

The cause of both syndromes is intimately associated with the formation of gas bubbles in the blood and tissues on decompression. Nitrogen forms only part of the content of these bubbles but it is the most important factor in both their initiation and maintenance. Aetiologically, the mass of bubbles originates in the watery tissues in the high-pressure syndrome, but in the fatty

tissues on exposure to altitude. In high-altitude decompression sickness susceptibility increases markedly with obesity but there appears to be no such correlation in the high-pressure syndrome. There is an increase in the incidence of high-altitude post-decompression collapse with increasing age.

In high-pressure decompression sickness, an increase of pressure involves an increase in the partial pressure of all the gases in the atmosphere, which may cause severally, carbon dioxide poisoning, nitrogen narcosis, and oxygen poisoning. The greatest hazard at altitude is lack of oxygen and little is known of the effect of anoxia itself on the decompression sickness syndrome, but most workers are subjectively convinced that oxygen-lack increases either its incidence, its severity, or both.

P. J. R. Challen

OCCUPATIONAL DISEASES

MINISTRY OF POWER. SAFETY IN MINES RESEARCH ESTABLISHMENT. **Safety in Mines Research, 1959** [RAMSAY, H. T., Director]. **38th Annual Report.** 66 pp., 13 figs. & 4 pls. [Numerous refs.] 1960. London: H.M. Stationery Office. [4s. 6d.]

This Report gives a detailed account of the work of the Safety in Mines Research Establishment during 1959.

As the result of extensive studies the phenomenon of firedamp roof layers is now understood. The formation of these layers is governed by a combination of the rate of emission of firedamp, the size and slope of the airway, and the speed of ventilation; and it is thought that some of the information given may become part of the essential knowledge of the ventilating engineer.

Engineering research has been much concerned with problems of haulage and suspension gear. It is often specified that the ultimate strength of components must be not less than so many times the static load; but this is not reliable unless supported by detailed stress calculations, for failure may be due to fatigue, and not simple static loading. This is illustrated by an account of work on the stresses in detaching hooks.

Work on explosives and blasting devices has been concerned with the hazards involved in millisecond-delay firing, and the danger of a firedamp ignition should a charge detonate when partly or wholly exposed is being studied. The work has shown that certain conditions are hazardous, and that, if the high standards of safety in shotfiring are to be maintained, explosives for general use in delay firing must be much less incendive than sheathed or Eq.S. explosives. Two other contributions to safety in delay shotfiring are the introduction into service of the new "lead element" short-delay detonators and the good results obtained in field trials of a 12-shot exploder.

In addition to the work on firedamp roof layers already mentioned, other work on the explosion hazard includes studies of aerosols for binding coal dust, of the physical properties of waterproofed stone dusts, and of other aspects of the use of stone dusts. There has been work on the aerodynamics and the mechanisms of coal-dust explosions, and on the ignition hazards from rocks, and on the safety of electrical circuits and equipment.

The weight of the existing types of 2-hour closed-circuit breathing apparatus for use in rescue work is usually between 30 and 40 lb., and it is complained that this is excessive. A reduction of weight is desirable, but the results of physiological studies have suggested that during heavy work in hot and humid conditions reduction of the temperature and humidity of the air inspired is even more desirable. A new liquid-oxygen apparatus developed at the Establishment provides relatively cool and dry air, and it weighs about 30 lb.

Part of the Establishment's work is directly concerned with the investigation of incidents and dangerous occurrences in mines. An Incidents Section has recently been set up to deal with the scientific aspects of actual underground explosions and fires.

In studies relating to pneumoconiosis much interest is being taken in the development of a gravimetric sampler for the measurement of respirable dust. Measurement of the mass concentration of such dust may prove to be more useful and more convenient than the current practice of measuring the particle-number concentration.

The counting and sizing of thermal precipitator samples is a highly skilled and tedious task. Automatic methods are highly desirable, and the report contains an interesting discussion of trials with an automatic counter.

In 1948, the National Coal Board agreed that men certified as having pneumoconiosis would be employed in places where the dust concentration did not exceed certain limits. One of the main objects of the Board's Pneumoconiosis Field Research Scheme, set up in 1953, was to obtain information as to the safety or otherwise of those standards, but the Scheme is unlikely to produce reliable results for another 5 to 10 years. Meanwhile, it is thought, the results obtained in a study of dust in haematite mines in Cumberland may give some indication. Between 1934 and 1937 an energetic programme of medical and dust control was instituted in these mines, and since then the dust conditions have remained much the same. It is claimed that of the hundreds of men who have entered the industry since 1937 none has been disabled by pneumoconiosis. Lung dust analyses have shown that the amounts of dust in different pathological grades are comparable to those found in coal-miners, and that the quartz content, although higher than that of coal-miners' lungs, is low compared with that found in silicosis. Dust measurements in haematite mines show concentrations that are considerably lower than the approved maxima for coal-mines.

The study of lung residues in coal-miners' pneumoconiosis shows that there is a fairly close correlation between the X-ray category and the amount and composition of the lung dust.

Thomas Bedford

AMOR, A. J. **One Generation. The Bridge Memorial Lecture, 1960.** *Trans. Ass. Indust. Med. Officers.* 1960, Oct., v. 10, No. 3, 74–9.

In *One Generation* Amor describes his experience of the changes in the two industries, nickel refining and coal-mining, with which he was associated during that period. He paints a vivid if depressing picture of the countryside and of the nickel works in South Wales as he first saw them. "The external environment in the valley was not good. The internal environment in the works was bad". The occupational hazards of coal-mining are summed up as sufficient to scare any man from the industry. The steps taken to reorganize the nickel industry so as to render the environment free from dust were the result of Amor's demonstration of the existence of cancer of the ethmoid, and lung, among the workers. A fine description is given of the first cases of these two conditions he encountered. The total number of deaths recorded in nickel workers at the factory was cancer of the lung 126, and cancer of the nose 62.

The industrial relations between management and workers in coal-mining in the early days was bad. The resistance of the men's agents to preventive measures is illustrated by their attitude to a proposed radiological examination of new entrants to detect tuberculosis. Amor was convinced, at an earlier date than most people, of the association of tuberculosis with massive fibrosis and was endeavouring to control infection. The wheel has gone full circle and such examinations are now carried out by the medical officers of the National Coal Board. The part to be played by research in future in the problems of industrial medicine is given full attention in the later part of the lecture. Provision made by the Factory Act for laboratories and other research services has yet to be fully employed. Fundamental research which adds to our scientific knowledge and develops new techniques is best dealt with by the universities, by the research departments of teaching hospitals and by the Medical Research Council.

A list of the variety of problems likely to be submitted for investigation shows that the cost of applied research will be very great. A laboratory sufficient for the purpose would cost not less than £1 million and the running costs not less than £250,000 per annum.

An ideal approach to one problem is cited in the case of papilloma of the bladder in the chemical industry.

The time is ripe for the Association of Industrial Medical Officers to formulate its ideas and to prepare the minds of those in authority for the establishment of such laboratories. *Charles L. Sutherland*

NATIONAL COAL BOARD. Medical Service. **Research on Medical and Allied Problems. Annual Report 1959** [ROGAN, J., Chief Medical Officer]. 14 pp. [11 refs.] [1960.] London: Hobart House, Grosvenor Place, S.W. 1.

This annual report, like its predecessors, is a useful brief summary of the research projects carried out during the year, and it contains some references to original papers in which full accounts of the work are given; these are published in the appropriate journals.

The studies involve statistical analysis of the incidence of sickness in miners, field research in pneumoconiosis and ventilatory function, the causation and treatment of complicated pneumoconiosis, bacteria in mine air, the beat diseases, knee injuries, fungus diseases, work in hot and humid conditions, and mines rescue work.

The accounts of these activities are very brief, but clear; they must be especially useful to the administrative officers of the National Coal Board.

Charles Wilcocks

MAY, K. R. **A Size-Selective Total-Aerosol Sampler, the Tilting Pre-Impinger.** *Ann. Occup. Hyg.* London. 1960, July, v. 2, No. 2, 93–106, 6 figs. (1 on pl.)

"A two-stage aerosol sampling unit is described in which a pre-impinger retains particles above the unit-density sphere diameter of 4–5μ and a backing impinger retains the remainder down to ca. $\frac{1}{2}\mu$. This division approximately simulates 'head' (upper respiratory) and 'lung' deposition in the respiratory tract. The pre-impinger is so designed that all the particles are impinged directly into liquid, to eliminate particle slippage, to aid the recovery of sensitive viable bacteria or viruses, to minimize internal wall losses and to give high particle intake efficiency, particularly in field conditions. A novel form of 'ideal' total-aerosol sampler is also described".

SÜSSE, W. Ein Beitrag zur gezielten Koagulation und Dispersion feinstkörniger trockener Mineralien. **[Observations on Coagulation and Dispersion of Fine Particles of Mineral Dust]** *Staub.* Düsseldorf. 1960, Dec. 1, v. 20, No. 12, 429–38, 22 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"Experiments have been undertaken on the influence of surface-active substances on dust-air mixtures. The particle size and electrical charges on the particles were first determined in a suitable apparatus. From the particle size distribution and the electrical charges it is intended to discover which surface-active substances give rise to coagulation or dispersion. It was possible to show in a series of experiments that coagulation or dispersion of the dust particles can be achieved as desired depending on the type and quantity of substance added. The change in the electrical charge on the particle is considered to be the cause of this phenomenon."

OLAF, J. Zur Verdampfung von Flüssigkeitsnebeln beim Staubmessen mit dem Tyndalloskop. **[The Evaporation of Mists in the Measurement of Dust with the Tyndalloscope]** *Staub.* Düsseldorf. 1960 Dec. 1, v. 20, No. 12, 440–45, 15 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"Measurement of dust in underground working in the coal-mining industry is disturbed by the occurrence of

aqueous salt solution mist. The magnitude and duration of existence of these mist droplets is discussed with reference to the measuring conditions in the 'tyndalloscope'. The dispersion of the mist can be achieved either by increasing the temperature or reducing the absolute humidity in the measuring chamber. Suitable apparatus has been developed at various places. Exhaustive testing has shown the superiority of the drying apparatus."

TALBOT, J. H. & KEMPIS, E. B. **Finely Ground Quartz: Evidence against a "Disturbed" Layer.** [Correspondence.] *Nature.* 1960, Dec. 10, v. 188, 927–9, 2 figs. [13 refs.]

HOUBERECHTS, A., DEGUELDRE, G. & CARTIGNY, S. Essai de détermination de la nocivité des empoussiérages miniers. Validité des mesures faites au précipitateur thermique. **[Estimation of the Toxicity of Mine Dust; the Validity of the Thermal Precipitator Data]** *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 2, 3–22, 7 figs. [34 refs]

The sole use of the thermal precipitator for dust sampling by the Belgian Institut d'Hygiène des Mines is justified on the grounds that it is possible to derive, from particle counts and microscopic examination for quartz content, a pneumoconiosis index which involves the mean square of the diameters of the quartz particles and the mean cube for the coal ones. It is considered necessary to include sizes between 5 microns and 0·5 micron rather than 1 micron since the omission of those below 1 micron makes it impossible to control the indrawn ventilating air and mechanical mining methods are increasing the proportion of fine dust.

The instrument is a standard Mk. III Casella. Bright field projection microscopy is used at 1,000 × magnification, with an immersion objective of n.a. 1·3. Intermittent sampling at 3·4 cm³ per minute is preferred to continuous, and individual exposures of 6–7 minutes are made at a rate of 4 or 5 in an hour. Experiments demonstrate how sampling for too long a period in relation to the dust concentration leads to superposition of particles on the slips and consequent under-estimation of the number (5–0·5 microns) and over-estimation of the average size; intermittent sampling helps to avoid this difficulty which is marked, even when obvious aggregates are broken down visually during counting since this cannot be done with complete success. It is considered that the dust deposit should have no more than 60–65 particles between 5 and 1 microns in a single traverse 40μ wide; this corresponds to 300 particles from 5 microns to 0·5.

The importance of using adequate magnification is indicated by a comparison of size distribution curves obtained at magnifications of 200, 500 and 1,000 X. When only particles smaller than 5 microns were counted 20 times more were recorded at the highest magnification than at the lowest. With the technique recommended an overall accuracy of ± 15% is claimed on the basis of special counting trials.

The content of free silica in the thermal precipitator sample is found by mineralogical methods which will not normally work for particles smaller than 5–6 microns but have been extended to smaller sizes by two methods. The first employs immersion in a liquid having a refractive index equal to that of quartz, at an intermediate wavelength, and depends on dispersion in the mineral producing colours under darkfield illumination. This is effective down to 2 microns. Alternatively, phase contrast is employed and operates down to 1 micron. The methods were checked against chemical analysis with satisfactory results.

The data obtained from these counting and mineralogical procedures are used to express the pneumoconiosis index, following French practice.

$$I = 3{\cdot}32 \log Ct - (10{\cdot}6 \text{ or } 8{\cdot}9)$$

where C is the number of particles per cm³ and t is the percentage of free silica. A graph of C against t indicates the danger zone for inhalation of silica-containing dust.

C. N. Davies

MARKS, J. & NAGELSCHMIDT, G. **Study of the Toxicity of Dust with Use of the *in vitro* Dehydrogenase Technique.** *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 383–9, 1 fig. [17 refs.]

The *in vitro* dehydrogenase technique of MARKS and JAMES [this *Bulletin*, 1959, v. 34, 903] was used to estimate the toxicity of a large number of dusts. The mean degree of dehydrogenase activity was plotted against the logarithm of the dose of dust, and the amount of dust per tissue culture required to depress activity to 50% of the controls' level, termed the toxic dose, was read off from the curve.

Fairly good agreement was found in comparing the toxicities of most dusts as estimated by this method with those obtained previously by studying tissue reactions in intact animals. Of the free silica dusts, tridymite and cristobalite were about equal and were most toxic—about twice as toxic as quartz. Some discrepancies were met which would make it hazardous to predict the behaviour of dust in man from its toxicity in cell cultures. For example, an impure Belgian quartz known to be of considerable fibrogenic activity was of relatively low *in vitro* toxicity. Treatment by hydrochloric acid, however, considerably enhanced this, probably by the removal of impurities, which, the authors suggest, might happen in the body over the course of years. On the other hand, calcium fluoride appeared to be more injurious in tissue culture than *in vivo* experiments would suggest, probably because of the liberation of fluoride ions. The confined conditions of tissue culture appears to be the factor involved in these discrepancies, on the one hand resulting in the retention of neutralizing impurities such as aluminium or iron, and on the other, preventing the removal of a dissolved toxic fraction. It appears that any relatively insoluble dust which proves to be moderately toxic *in vitro* is likely to be fibrogenic *in vivo*: less active dusts should be treated with acid before testing in tissue culture to imitate the long continued leaching action of the body fluids.

The particle size range of the samples of dust examined was between 0·5μ and 2μ. Particles less than 0·5μ tended to adhere to one another and gave varying degrees of dispersion in different experiments. Toxicity did not

relate directly to surface area. The number of particles per cell was surprisingly low—less than unity in many cases and never exceeding 4. This suggests to the authors that during the 3-day period of incubation, cells which have taken up dust may die and be ingested by other cells which are damaged in turn.

On the basis of the results obtained the authors advance an interesting hypothesis; that the primary dust lesion stems from injury to the macrophages, not to connective tissue, and that there is a combination of an essential cell constituent, probably a protein, with the surface of the particles. *A. T. Doig*

MARKS, G. S. & MARASAS, L. W. **Changes in the Lung Lipids of Rabbits and Guinea-Pigs exposed to the Inhalation of Silica Dust.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 31–5. [23 refs.]

This investigation, which was carried out in Johannesburg, was concerned with the possibility that lung lipids play a part in the formation of silicotic lesions. Previous work by STRACHAN and SIMSON (*Records of the International Conference held at Johannesburg*, 1930, Geneva; ILO, p. 231 [this *Bulletin*, 1931, v. 6, 513]), had shown an increase in lipid with advancing fibrosis. Rather similar findings had been described in experimental tuberculosis and it seemed likely that, after cell death in silicosis and tuberculosis, there is a release of phospholipid material which produces the lesion.

8 rabbits and 24 guineapigs were exposed to a silica dust cloud of about 40,000 particles per ml., of which about 97% were less than 2·2μ, and killed, with unexposed controls, at 4-week intervals up to 30 weeks. In the guineapigs there was a steady rise in the silica content of the lungs, of the wet and dry lung weights in those exposed for longer than 12 weeks, and of the total and phospho-lipids. Lecithin, total cholesterol and free cholesterol all took part in the increase. Collagen increased slowly and was always greater in the lungs of experimental animals than in those of the controls, but the ratio of collagen to lipid is difficult to ascertain as the amounts are shown in different tables and no graphs are given.

In rabbits, unlike the findings of FALLON (*Canad. Med. Ass. J.*, 1937, v. 36, 223) there was no generalized increase in lipid or phospho-lipid. The likely explanation is that the silica did not reach the lungs in sufficient quantity, and it is pointed out that in laboratory conditions, the activity of rabbits, and therefore their respiratory minute volume, is low, whereas the guineapigs are able to be much more active. Fallon administered the silica by intratracheal injections in his experiments.

A. T. Doig

NAGELSCHMIDT, G. **The Relation between Lung Dust and Lung Pathology in Pneumoconiosis** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 247–59, 3 figs. [Numerous refs.]

Methods of isolation and analysis of dust from pneumoconiotic lungs are reviewed. The results of lung dust analyses for different forms of pneumoconiosis, as recorded by research workers in countries throughout the world, are cited. The findings of these workers are combined in a series of tables. The tables record the average amount and composition of lung dust according to severity of pneumoconiosis.

Table 2, classical silicosis (6 references)
Table 3, pneumoconiosis of coal-miners (2 references)
Table 4, in lungs which contained almost no quartz (11 references)
Table 5, foundry workers' lungs (1 reference)

Following this review of his own researches and those of others the author advances a tentative classification which separates beryllium, aluminium, abrasive fume, and asbestos, which cause interstitial or disseminated fibrosis, from quartz, coal, haematite, talc, kaolin, and other dusts, which cause a nodular or focal fibrosis which may change to forms with massive lesions. The data suggest that in the first, but not in the second, group the dusts are relatively soluble; only in the second group do amounts of dust and severity of fibrosis go in parallel for a given form of pneumoconiosis. In classical silicosis the quartz percentage is higher and the amount of total dust much lower than in coal-miners' pneumoconiosis. Mixed forms of both groups occur, for instance, in diatomite workers. *A. Meiklejohn*

LABELLE, C. W. & BRIEGER, H. **The Fate of Inhaled Particles in the Early Postexposure Period. II. The Role of Pulmonary Phagocytosis.** *Arch. Environment Health.* Chicago. 1960, Nov., v. 1, No. 5, 423–7, 6 figs.

A technique is described for estimating the number of free phagocytic cells in the lungs of rats by washing out the excised lung and trachea with isotonic saline solution and counting the cells under the microscope.

Previous experiments had shown [this *Bulletin*, 1959, v. 34, 1260] that the elimination of particles from the lungs of rats took place in two stages, an early postexposure one in which 40% of the total dose was eliminated with a half-life of 17 hours, followed by a slower clearance.

It is now found that the fraction of the total dose eliminated in the early period is proportional to the number of phagocytes in the lungs. Increasing the amount of dust administered results in an increase in the percentage cleared but the half-life remains about the same. An increase in the phagocyte count follows immediately after the commencement of dust inhalation and attains a maximum in about 10 hours. The count then falls exponentially with a half-life of 19 to 25 hours.

It is concluded that the particles are removed from the lung by phagocytes and that this is the normal clearance process, stimulated by the arrival of dust particles in the alveoli. Only few, atypical, dust-laden cells remain behind for detection in lung sections by conventional histological technique.

The phagocytic reaction following intratracheal injection was identical with that resulting from inhalation as long as too much dust was not administered. It is suggested that a burden exceeding 1·5 mgm. per rat lung blocks phagocytic clearance. [See also *ibid*, 1960, v. 35, 106.] *C. N. Davies*

NORVITT L. Individuelle Disposition für Silikose. Lymphogene Lungenreinigung und Tuberkulose. **[Individual Differences in Susceptibility to Silicosis. Lymphatic Clearance of the Lungs and Tuberculosis]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 463–84. [Numerous refs.]

Susceptibility to silicosis varies greatly among individuals, for it is observed that there is no good correlation between the duration of exposure to dust and the time of onset and severity of silicosis even when the extent of dust exposure and work conditions are identical. This individual disposition must be dependent on endogenous factors: many suggestions about these have been given in the literature and these are listed in this paper. The analysis of many of the factors has not as yet explained individual disposition. The author of this paper considers only the important factors of lung clearance by the lymphatic system and the interaction of tuberculosis and silicosis. These are described and discussed at length with reference to the extensive literature.

The opinion expressed by the author is that tuberculous pulmonary infection plays an important role in individual susceptibility to silicosis. The lymphatic system protects the lungs by clearing them of inhaled dust which ultimately reaches the blood stream. In similar fashion the lungs are cleared of bacteria and in persons who breathe a dusty atmosphere and acquire tuberculous infection the lymphatic system is put to the extra strain of removing tubercle bacilli and hence the dust particles are removed less efficiently. The extent to which tuberculous infection may increase susceptibility to silicosis depends on the stage of the infection and the danger is greatest in the primary stage.

Tuberculin negative persons are the least at risk of silicosis but are at the greatest risk if exposed to tuberculous infection. Regular tuberculin tests of such persons should be carried out and if the test becomes positive they should be removed from exposure to silica dust for the time being. BCG vaccination of the tuberculin negative should not be carried out while workers are exposed to dusts but a long time before they begin such work. *M. E. Delafield*

SCHWARZ, W. Elektronenmikroskopische Untersuchungen an Fibrillen und Kittsubstanz normaler und silikotischer Lungen. **[Investigation by Electron Microscope of Fibrils and Cement Substance in Normal and Silicotic Lungs]** *Beiträge z. Silikose-Forschung.* 1959, No. 63, 1–20, 5 figs. [19 refs.]

The reticulin fibres of the connective tissue of the lungs have two fundamental components, fibrils and cementing substance. The thickness of fibrils was investigated by the electron microscope. It was found to be about 350Å as an optimum but steadily diminished after the age of 50 years. This diminution when plotted graphically occurs in a straight line both in normal and silicotic fibrils. Since there is no connexion between the severity of the silicosis and this decline in thickness, it is clear that the silicotic fibrils are not different qualitatively from normal lung fibrils, but are quantitatively increased. STACY and KING (*Die Bestimmung von Kollagen im fibrotischen Gewerbe. Die Staublungenerkrankungen* 3. Dr. D. Steinkopff-Verl, Darmstadt, 1958) are quoted as showing that the collagen content of the silicotic nodules of rats was 6 times higher than in normal lungs of rats.

The cementing substance consists of granular elements which are deposited round the fibrils. It is not amorphous, and the electron microscope allows the individual elements of the interfibrillary substance to be investigated. The chemical structure of the cementing substance is discussed, and the role of the mucopolysaccharides is considered.

The cementing substance undergoes both a qualitative and a quantitative change in silicotic fibres. It is very strongly bound to the fibrils and its density may make them obscure in the electron microscope. The hyaline appearance is due to a change in the cementing substance and this effect is linked to an increase of mucopolysaccharides.

Schwarz thinks that sufficient consideration is not given in silicosis research to the presence of the two fundamental structures in normal and silicotic fibres and to the different changes they undergo. He proceeds to discuss the part they may play in the various theories of silicosis. A paper by SCHWARZ and MERKER on the use of the electron microscope [this *Bulletin,* 1959, v. 34, 133] should be consulted. *Charles L. Sutherland*

NORDMANN, M., KOCH, W & MÄDER, Ellen. Die Resorption einverleibten Staubes. Spätstadien reiner und gemischter Stäube: Kieselgur, Quarz, Kieselgur und Quarz. **[The Absorption of Dusts introduced into the Body: Late Stages in Pure and Mixed Dusts]** *Beiträge z. Silikose-Forschung.* 1959, No. 63, 21–33, 3 figs.

This appears to be a continuation of investigations by LÖBLICH *et al.,* [this *Bulletin,* 1959, v. 34, 348, 546]. The studies with kieselguhr on rabbits showed that no fibrosis resulted after 4 months. The present investigations on kieselguhr were continued for a period of 13 months. Similar investigations were also carried out with quartz alone and with a mixture of quartz and kieselguhr. The dusts were suspended in physiological salt solution and injected between the folds of the mesentery. The effects were observed with the intravital microscope: and at the end of 13 months the histological changes were examined in the mesentery in the regional aortic lymph nodes.

With kieselguhr alone, deposits were found in the mesentery to consist of large multinucleated giant cells which contained most of the dust. There was very little production of fibrous tissue and no evidence of concentric fibrosis. Rarely evidence of dust was found in lymphatics or lymph nodes but traces of a brown material giving the iron reaction were found. It is concluded that the removal of kieselguhr from the body is only a question of time, and of the amount of dust injected.

With pure quartz, the dust used had a particle size of 4 microns or under. No difference could be found during life between the granulomata produced by quartz and those by kieselguhr. The histology of quartz granulomata however showed a much greater fibrosis. The giant cells were smaller, more regular in form and had a smaller number of nuclei; they were full of polarizable crystals. The fibrotic reaction ranged up to typical silicotic nodules.

The two types of reaction to kieselguhr and quartz are therefore easily distinguished.

When kieselguhr and quartz were injected together, the two types were found. These dusts act on the tissues side by side according to their properties. The typical tissue changes arise independently of one another and no evidence of the production of a special reaction was observed. There is however a statement that in human pathology, it can be presumed that mixed dusts may produce a fibrosis which is responsible for the morphological variations of human pneumoconiosis.

Charles L. Sutherland

PERNIS, B., VIGLIANI, E. C. & MONACO, L. **A Study of the Action of Silica Particles on Macrophages *in vitro*.** *Med. d. Lavoro.* 1960, Jan., v. 31, No. 1, 3–9, 2 figs. on pl. [23 refs.]

It is widely held by research workers that degeneration of mononuclear phagocytes plays a fundamental role in the pathogenesis of silicosis. This viewpoint is based mainly on *in vivo* experiments in which quartz particles were injected parenterally. Arising out of such investigations Vigliani and Pernis of the University of Milan advanced the hypothesis that the observed immunological and fibroblastic reactions, which lead to the formation of silicotic nodules, are not the direct consequence of silica in the tissues, but are due to substances released from the degenerated phagocytes. To throw further light on the crucial steps in the pathogenesis of silicosis associated with the degeneration of phagocytes they designed *in vitro* experiments. For this purpose they adapted the culture chamber technique developed by MACKANESS [this *Bulletin*, 1953, v. 28, 612] to study the action of tubercle bacilli on rabbit peritoneal exudate macrophages. The authors summarize their findings as follows:

"The action of silica dusts on macrophages 'in vitro' has been studied with the culture chamber technique of Mackaness (1952) on rabbit peritoneal macrophages.

"Extensive morphological alterations of phagocytes incubated with Tridymite or HF- etched Quartz take place in the first 24 hours; these alterations consist of a marked swelling of the cytoplasm, that assumes a watery appearance, and extreme distension, followed by rupture, of the cell membrane. These alterations resemble those induced in cell cultures by active complement. It is possible to prevent the appearance of morphological alterations of macrophages incubated with Tridymite under conditions that inhibit complement such as low temperature (2°C) and suitable dilutions of various complement inhibitors (48/80, GSH, TAMe).

"The possibility is then considered that the lysis of macrophages that have phagocyted quartz particles, is due to activation of complement or of a complement-like enzymatic system. In this respect the most likely alternative of complement seems to be the non-specific esterase which is present in the cytoplasm of the macrophages."

[The following announcement is made in this issue of *La Medicina del Lavoro*:

"In order to extend among foreign research workers the knowledge of the contribution of Italian doctors to the researches on Occupational Health, the Editor of this Journal has decided to accept also papers written in English, French or German, beginning with the present issue. Papers written in one of the above languages and submitted for publication by foreign authors are also welcomed."

English readers will, I am sure, welcome this policy. May I respectfully submit that in articles and summaries in English, English as opposed to American spelling should be followed, *e.g.* fibers should be written fibres.]

A. Meiklejohn

CHATGIDAKIS, C. B. **Nodular Muscular Hyperplasia in the Lungs of South African Miners.** *Arch. Indust. Health.* Chicago. 1960, Feb., v. 21, No. 2, 160–64, 4 figs. [24 refs.]

In the normal lung smooth muscle is confined to the walls of blood and lymphatic vessels, the bronchi, bronchioles and alveolar ducts. There is no smooth muscle either in the pleura or interstitial tissue of human lungs under normal conditions. The occasional occurrence of smooth muscle in these situations was first described by VON BUHL in 1872 and since then the condition has been variously named muscular hyperplasia, muscular cirrhosis of the lungs and pulmonary myomatosis.

In the course of post-mortem examination of miners' lungs at the Pneumoconiosis Research Unit, Johannesburg, during the short period of 5 months, 30 examples of nodular muscular hyperplasia of the lungs were observed. 26 cases occurred in African labourers and 4 in Europeans; 26 were gold-miners and the rest coal-miners. The macroscopic and microscopic appearances of the lesions, including the identification of muscle tissue by appropriate staining techniques, are described. The significance of these nodules has not so far been determined but their frequency in miners suggests, it is stated, an aetiological relationship to dust exposure. The author thinks that the muscular nodules may arise from hypertrophied lymphatic vessels. A case is described to show that this nodular muscular hyperplasia may be confused radiologically and at necropsy with true silicosis.

[This is an interesting addition to pneumoconiosis literature.]

A. Meiklejohn

POLACHEK, A. A. & PIJANOWSKI, W. J. **Extrathoracic Egg-Shell Calcifications in Silicosis.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 714–20, 7 figs. [15 refs.]

Two men with silicosis presented with radiological evidence of egg-shell type of calcification both within and outside the chest. One was a sand-blaster who had the characteristic calcifications in his abdomen and a calcified gland was felt in the right supraclavicular region. The second man had worked in coal-mines and in a stone mill. He, likewise, had the calcification in the right supraclavicular region and in the abdomen. The silicotic nature of the lesions was confirmed histologically. The abdominal distribution was explained by retrograde lymphatic carriage of silica particles, and the supraclavicular involvement by the normal drainage from the

lung. The authors dismissed tuberculosis as a contributory factor but they make no reference to cases of egg-shell calcification described in the literature in which there had been no silicosis. *J. Gough*

HOLT, P. F. & WENT, C. W. **Studies on the Nature of Silicosis: A Suggested Mechanism of Fibrogenesis.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 25–30, 5 figs. [23 refs.]

"One theory which seeks to explain the production of fibrous tissue in silicosis postulates the interaction of collagen precursors with polysilicic acid. This stage has been questioned because it is doubtful whether polymerized silicic acid is normally formed when quartz dissolves in aqueous media. A mechanism by which silicic acid may be polymerized *in vivo* has been demonstrated by studying the properties of polyamide monolayers, which behave like collagen monolayers when spread on silicic acid substrates. The silicic acid which is adsorbed beneath the monolayer polymerizes when the polyamide films are subjected to pressure.

"In fibrogenesis, the polysaccharides which are produced in large amounts may serve to prevent the premature agglomeration of the collagen units. Later, when the concentration of the polysaccharide is largely reduced, the polysaccharide may assist in aligning and cementing the units together to form fibres. The physiological process is probably reversible but, if silicic acid takes the role of the polysaccharide in this second stage, the building up of fibres is likely to be an irreversible process."

GROSS, P. **Current Concepts of Pneumoconiosis. Pathological Aspects.** *J. Amer. Med. Ass.* 1960, Feb. 6, v. 172, No. 6, 546–9. [17 refs.]

The author discusses the theories concerning the behaviour of dust in the lungs and the onset of fibrosis and summarizes the modern conception of the various mechanisms, giving principal references, as follows.

Adequate respiratory excursions play an important role in keeping the alveoli clear. Naked, as well as ingested particles may pass through the alveolar membrane, assisted by intra-alveolar fluctuating pressures, and alveolar excursions; certain drugs may facilitate their passage and also an excess of carbon dioxide. Silicotic nodules begin not in the perivascular spaces but in alveolar spaces surrounding the vessels, and the silica-bearing cells are believed to be proliferated alveolar cells. Dust in the lung tissue may be mobilized and begin its fibrogenic activity at a new site. The solubility theory has been all but abandoned: the present theory is that silica crystals possess a surface activity which denatures cell proteins. As beta and gamma globulins form a significant component of silicotic nodules their deposition is believed to indicate a subsequent immune reaction. Other dusts than silica, for instance coal, kaolin, aluminium oxide and silicon carbide may be associated with the development of massive fibrosis, and as this condition is considered to be due to tuberculous infection, the author advocates the use of the generic term "tuberculopneumoconiosis". The mechanism of the development of emphysema in dust conditions is not yet clear. *A. T. Doig*

VAN MECHELEN, V. Nouvelle classification internationale des radiographies des pneumoconioses (Genève 1958). [**New International Classification of Radiographs of the Pneumoconioses (Geneva, 1958).**] *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 2, 23–34, 1 diagram. [Flemish version 35–40. (10 refs.)]

See this *Bulletin,* 1960, v. 35, 21.

WAGNER, J. C., SLEGGS, C. A. & MARCHAND, P. **Diffuse Pleural Mesothelioma and Asbestos Exposure in the North Western Cape Province.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 260–71, 12 figs. [34 refs.]

[Based on clinical, post-mortem and epidemiological studies it is widely, but not universally, accepted that there is an aetiological relationship between asbestosis and cancer of the lung. The closeness of this association seems to differ with the variety of asbestos, chrysotile, horneblende and crocidolite [this *Bulletin,* 1955, v. 30, 780].

At necropsy in cases of asbestosis a dominating feature of the pathological changes in many cases is the extensive thickening of the pleura with plaque formation (*ibid.*, 1933, v. 8, 811). These pleural changes are reflected in the characteristic radiological appearances of the disease.]

Crocidolite (Cape blue) asbestos was discovered in the north-west Cape Province of the Union of South Africa about 1806. Since then prospectors have established that "Asbestos Mountains" covering an area of approximately 8,000 square miles extend more or less northwards from near Prieska between longitudes 22·30° and 23·00° E. Mining operations began in the Prieska district about 1893 and gradually spread northwards. Initially the ore was quarried in open-cast workings and later in shallow drift mines. The quarrying was a family business undertaken by the local inhabitants. Separation or cobbing of the fibre from the associated ironstone was done by hand, often by women who were accompanied by their infants and young children. In this way whole families were exposed to the inhalation of asbestos dust, as also were persons living in the area. Owing to urgent demands for supplies of crocidolite during the war, 1939-45, mining companies were formed. They developed deeper workings and set up mills to crush the ore.

In February, 1956, the Pneumoconiosis Research Unit at Johannesburg observed at necropsy a case of mesothelioma of the pleura in a case of asbestosis. This was significant as mesothelioma is a rare tumour not only in South Africa but throughout the world. In fact some pathologists have denied its existence. The combination with asbestosis in this case might have been entirely coincidental and not of direct causal relationship. But during the early months of the same year, 1956, one of the authors of this article, Dr. C. A. Sleggs, who practised in the North Cape Province, treated no less than 6 patients with gross pleural thickening. Lung biopsy in 2

of these cases showed the features of mesothelioma. In the ensuing 2 years 8 additional cases occurred in the same neighbourhood and 5 elsewhere in the Union. The possibility that exposure to asbestos might be a causal factor was suggested by the fact that the first case was accompanied by asbestosis and 10 of the other cases were referred to hospital from a large asbestos mining area. These observations stimulated the present inquiry. 33 cases (22 males and 11 females, ages 31–68) of diffuse pleural mesothelioma were collected and with 1 exception all had been exposed to the inhalation of asbestos dust (crocidolite). The series included workers at the mines, transport men and individuals living in the vicinity of the mines and mills. Details of the individual cases are tabulated; the items include year of birth, age at diagnosis, race, sex, asbestos exposure, diagnosis (biopsy or necropsy or both), histology and period of survival in months after diagnosis. 6 patients are still alive and in the 27 fatal cases the survival period varied between 5 and 48 months, mean 14·6 months. According to an addendum 2 months after the submission of manuscript the number of cases observed had increased from 33 to 47. In 45 of this total there was a possible exposure to crocidolite. In 1 case a mesothelioma of the peritoneum was present.

8 of the cases are described in detail and the article is excellently illustrated by pathological and histological specimens and radiographs.

The authors, quite reasonably, regard the findings as highly suggestive of an aetiological relationship between mesothelioma of the pleura and exposure to crocidolite asbestos. Nevertheless they emphasize that the evidence is not conclusive and so wish this paper to be read as a preliminary communication.

[The authors are to be commended for this original and continuing study. At the Pneumoconiosis Conference (see *Proceedings of the Pneumoconiosis Conference,* South African Council for Sci. and Indust. Res., London, 1960, J. and A. Churchill Ltd.) held at the University of Witwatersrand in 1959, Dr. J. C. Wagner gave a preliminary account of this work. Among the final recommendations adopted by the Conference was the following (No. 12):

"That the relationship between exposure to asbestos and mesothelioma of the pleura, which appears more prevalent in South Africa, should be further investigated.

"This investigation would be facilitated by the establishment of a central registry of cases under the South African Council for Scientific and Industrial Research." (Address P.O. Box 4788, Johannesburg, South Africa.)

Between 1930 and 1946 I attended many necropsies on cases of asbestosis. These derived from a factory engaged in the processing and fabrication of asbestos textiles from crocidolite (Cape blue) asbestos. An outstanding feature of many of these cases was the gross thickening of the pleura. The appearance was peculiar in that the whole lung seemed to be uniformly ensheathed in a cuirass up to ½ inch thick. Professor J. Gough, Cardiff, has produced beautiful large sections of such cases, in which this cuirass is displayed by differential staining. Only once do I recollect that Dr. S. R. Gloyne reported the pleural condition as malignant. A search of the original reports and sections at the London Chest Hospital might now produce some interesting observation.] *A. Meiklejohn*

Böhme, A. Asbestose und Lungencarcinom. I. Mitteilung. [**Asbestosis and Cancer of the Lung. 1st Part**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 4, 384–95, 2 figs. [16 refs.]

The first communication deals with the results of the periodical examinations of 250 workers in an asbestos factory. Examinations carried out at intervals of 1 or 2 years revealed 92 cases of asbestosis. Investigations of a similar type had already been carried out in Dresden by Bohlig and Jacob [this *Bulletin,* 1956, v. 31, 648] and by Braun and Truan [*ibid,* 1958, v. 33, 1142]. The 92 cases comprised 32 in stage 0–I, 26 in stage I, 14 in stage I–II or II, and 20 in stage II–III or III. 6 patients had died of asbestosis and cancer of the lung. Autopsies were performed in all 6 and details of each are given in full. The reports of the autopsies confirm the known fact that carcinoma in asbestosis cases is generally localized to the parts most affected by the asbestosis namely, the lower lobes. In contrast to the usual experience only 1 was a squamous carcinoma, the others being either of an adenomatous or of the undifferentiated type. The carcinoma appears to arise from several centres; in 4 of the subjects metastases were present. In one patient, the cancer was not recognized during life; the appearance of a tumour may be masked by the radiological changes produced by the asbestosis. Even at post-mortem examination, the diagnosis of neoplasm may depend on the histological examination.

The age at death was on the average 51 years and the average duration of exposure was 29 years. Cancer appears in patients with asbestosis in later life and after the asbestosis has existed for many years. The author agrees that his figures are too small to allow a definite conclusion. *Charles L. Sutherland*

Böhme, A. Asbestose und Lungencarcinom. II. Mitteilung. [**Asbestosis and Cancer of the Lung. 2nd Part**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 457–62.

In the first communication, 6 cases of carcinoma were described as occurring in 92 cases of asbestosis, but if the very mild cases are omitted the figures are 6 cases in 60 (10%). The author now extends his study by using data supplied by the Textile and Clothing Trade Company, Augsburg. This Company covers the insurance of the asbestos factories of north Germany with the exception of the Frankfurt area. Subjects compensated under the Fifth Regulation, No. 28 (asbestosis) and No. 28b (asbestosis in combination with carcinoma of the lung), numbered 125 during the years 1952–58. There were 31 deaths during that period and post-mortem examinations were performed on 20. In 11 of these the diagnosis of carcinoma was verified. In 7, other causes of death were found and 2 remained uncertain. In one case of the 11 not submitted to post-mortem the cause of death was given as carcinoma of the lung. In half of the verified cases of carcinoma, the condition was diagnosed or suspected during life. In a further case where the patient was still alive the diagnosis was made by resection of the lung.

Of the 125 subjects with asbestosis 63 were women and 62 men. Carcinoma was verified in only 2 of the

14 women who died, but it was found in 12 of the 17 men who died. Heavier smoking and more intense exposure to dust in men may account for this difference in incidence.

Carcinoma might have developed in a few of these persons even if there had been no asbestosis, and this might have been the case where there was a new growth of the pleura with only mild asbestosis. Moreover, in a few cases the tumour was in the unaffected upper lobes. But in general the results point to a causal connexion between the presence of asbestosis and the appearance of a carcinoma. This is admitted in the wording of No. 28b of the Fifth Regulation.

Charles L. Sutherland

Kipling, M. D. & Bech, A. O. **Talc Pneumoconiosis.** *Trans. Ass. Indust. Med. Officers.* 1960, Oct., v. 10, No. 3, 85–93, 11 figs.

Talc is a hydrated magnesium silicate ($Mg_3SiO_4O_{11}\cdot H_2O$ or $3MgO\cdot 4SiO_2\cdot H_2O$). Talc is related to both asbestos and mica, the commercial form contains no free silica. Investigations in America in the 1930s left little doubt that talc dust could give rise to a pneumoconiosis on its own account. Merewether [this *Bulletin,* 1934, v. 9, 230] and McLaughlin [*ibid,* 1949, v. 24, 975] investigated the disease in the rubber industry. It may be said that at present anyone working with rubber is liable to be exposed to talc dust but cases only occur when evolution of dust is high; the proportion affected is small. Cases have occurred in the pottery industry in the manufacture of the insulation of pylons, in the paper industry and the manufacture of lead accumulators. Talc produces characteristic bodies in the lesions similar to those found in asbestosis, but the author is not satisfied that every talc pneumoconiosis should be included with asbestosis in the category of fibrous silicatosis.

Details are given of 7 cases comprising 4 lead casters, 1 tyre extruder and 2 who had dusted or sprayed aluminium castings. It is unfortunate that the results of physiological tests, particularly those indicating the possible presence of alveolar capillary block, are not included.

Charles L. Sutherland

Agnoletto, A. & Fabbiocchi, P. A. Febbre da inalazione di polvere di madreperla. **[Fever caused by the inhalation of Mother-of-Pearl Dust]** *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 612–23. [12 refs.] English summary.

This is a long and detailed report on one patient who after having worked at making buttons of mother-of-pearl for 5 years began to have febrile attacks in the afternoons, these attacks occurring one or more hours after he had restarted work after the midday break. The attacks, which at first were occasional, gradually became daily and consisted of fever up to 39°–40°C. with shivering and headache. No other signs or symptoms were found and there were no organic changes. The attacks stopped when he was transferred to other work, only to start again when he returned to button-making. The condition was therefore regarded as definitely occupational but in spite of the most intensive clinical and especially laboratory investigations, including inhalation of aerosols of mother-of-pearl dust, patch testing of the intact and scarified skin, the use of antihistaminics etc., no allergic condition was found, though *inter alia* the investigations showed that the concentration of Zn in the dust of the particular shell used (*Trochus macassar*) was very much higher than has been reported in the literature hitherto, while again 50% of the dust particles were less than 1μ in size, also not previously reported.

No final conclusion was reached as to the aetiology except that it was definitely occupational, and no similar case has been found in the literature.

W. K. Dunscombe

Gross, P., Westrick, Marian L. & McNerney, J. M. **Glass Dust: a Study of its Biologic Effects.** *Arch. Indust. Health.* Chicago. 1960, Jan., v. 21, No. 1, 10–23, 9 figs. [10 refs.]

The authors made a comprehensive investigation of the effects of glass dust on the conjunctiva, gastro-intestinal tract and lungs of guineapigs and rats.

In the study of possible eye irritation the conjunctiva was dusted with finely milled glass flakes of average thickness 5μ and mostly less than 50μ in diameter. No ill effects were demonstrated.

In the ingestion studies, similar milled glass flakes to the amount of 10% in one group of young rats and 50% in another were added to the normal diet for one year. There were no significant changes in health. All of the 10 rats which ingested such massive doses of glass as the equivalent weight of their daily food survived the year's experiment. Post-mortem examinations in both groups showed no abnormalities.

The pulmonary studies consisted of intratracheal injections of coarse glass suspended in corn oil, of corn oil itself, and of fine glass (mean diameter 1·1μ), quartz and kaolin, each suspended in water. [Corn oil had to be used as the suspending medium for the coarse glass to counteract the rapid settling which occurred in water.] 15 rats were used for each type of injection, 3 being killed from each group at the end of 6 months and survivors at the end of 12 months. Inhalation studies were also conducted with fine glass, quartz and kaolin on 3 groups of 40 rats and 3 groups of 15 guineapigs, exposures continuing for one year and examinations being made at 6 months, one year and two years after starting exposure.

The pulmonary reactions to both coarse and fine glass were minimal and consisted of small focal alveolar collections of macrophages with a little proliferation of alveolar lining causing slight thickening of alveolar walls. The lesions are described as non-fibrogenic although in some a few collagen fibres were noted. Glass dust deposits in lymph glands were completely inert. Quartz produced less marked lesions than expected, silicosis being not apparent or very slight on naked eye examination, while microscopically the consolidations were more cellular, irregular and contained less collagen. The lesions produced by kaolin were similar to but slightly more severe than those produced by glass dust. The possible reason for the unexpected inhibition of silicotic fibrosis

from quartz may be that, by the method of preparation, all the fine dusts, glass, quartz and kaolin contained a good deal of iron (amounts not stated).

[It seems to the reviewer therefore that because of this unfortunate contamination no firm conclusions as to pulmonary effects can be made from these otherwise careful experiments, although the results of the studies on the effects of coarse glass dust on the eyes and after ingestion can be accepted.] *A. T. Doig*

EHRHARDT, W. & HEIDEMANN, W. Zur Klinik und Pathologie der Ockerstaublunge. **[Pneumoconiosis from Ochre Dust: Clinical and Pathological Observations]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 504–18, 14 figs. (4 coloured).

Opinions on whether the lungs of workers in ochre dust may reveal true silicotic lesions have been divided. This paper reports at considerable length on the fatal case of a man who worked for many years in an ochre pigment factory. His personal and medical histories are given with an account of clinical findings and description and X-ray photographs of the lung condition. A full post-mortem examination was made and the findings are described with a number of photographs of the macroscopic and microscopic appearances of the lungs.

These appearances were regarded as being those of a true silicosis although the presence of the changes of a siderotic nature which were also seen is not surprising in view of the high content of iron in ochre dust.

M. E. Delafield

ANTWEILER, H. Tierexperimentelle Untersuchungen zur Pathogenese der Byssinosis. **[Investigation of the Pathogenesis of Byssinosis by Animal Experiments]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 17, No. 6, 574–88, 8 figs. [14 refs.]

The material for the experiments was obtained from a Dutch cotton spinning factory in which American, Indian and Egyptian cotton was used. Raw cotton dust under the microscope shows impurities recognizable as parts of the plant, probably broken pieces of the seed capsule and seed pod. The dust from the air of the carding-room consists not only of threads of cotton but also to a great extent of the same parts of the seed. Crystalline particles are seldom found. Waste found under the carding machine consists mostly of the same remains of the seed capsule; the proportion of cotton itself is very slight. Waste from the other parts of the factory dealing with carded cotton, contains scarcely any of the impurities; it consists mostly of fine cotton and of added material. From these dusts extracts were prepared by a method which is described in detail. These extracts on being tested were shown to contain no protein. A series of experiments with these extracts were performed on rats, cats, rabbits and guineapigs. The histamine content of each extract was estimated on portions of guineapig ileum.

The peritoneum of rats is normally rich in mast cells with a high histamine content which is reduced by the action of liberator substances. Experiments with rats showed that raw cotton dust and dust from the carding-room produced this effect. A second injection, 4 hours later, only resulted in half the amount of liberated histamine.

Blood pressure and changes in breathing were studied by intravenous injection in cats. A fall in pressure, similar to that of the histamine-liberating compound 48/80, was produced by a dose of extract of 1–2 ml. Along with the drop in blood pressure the breathing became shallow, to return to normal later with the blood pressure. The blood of cats showed an increase of free histamine after injection of extracts, returning to normal in 30 minutes. The plasma was then tested on guineapig bowel, producing a contraction showing that apart from histamine a slow-reacting substance was present.

Rabbit blood plasma to which extract had been added and then incubated at 37°C. showed an increase of histamine action 10 times that of control plasma. In living rabbits the content of platelets was lowered after injection of extract.

The conclusion is that raw cotton dust, dust from the air of the carding-room and from the waste from the carding machine, contain a substance which can liberate histamine and probably another substance from mast cells. The dust from other parts of the factory where purified cotton was used contained none or very small amounts of this liberating substance. As the dusts containing this substance are composed mostly of seeds and the remains of seed capsules, it can be assumed that these parts of the plant contain the active substance. As sufferers from the inhalation of cotton come from the carding-room, there appears to be a connexion between the bronchial symptoms of the cardroom worker and the presence of this liberating substance in the dust.

The freeing of histamine does not result in the destruction of the mast cells; the cessation of inhalation over the week-end gives the cells time to replace their store of histamine. Hence the symptom called Monday fever. The dyspnoea of carding-room workers appears only after work in the process has exceeded 5 years. The explanation suggested for this delay in the appearance of symptoms is that irritation of repeated and lasting inhalation of dust produces an increase of mast cells in the region of the air passages. Thus the amount of histamine ready for liberation is increased.

Charles L. Sutherland

POLLAK, K., GUTHERT, H. & SCHANZENBACH, H. Experimentelle Untersuchungen zur Frage der Getreidestaublunge. **[Experimental Investigation of Grain Dust in the Lungs]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 519–30, 5 figs. [31 refs.]

DUNNER and HARDY [this *Bulletin*, 1952, v. 27, 125] showed that radiological changes varying from increased reticular markings to miliary shadows may be found in dock workers in Britain, who are exposed to grain dust. Grain dust similar to that to which the dock workers are exposed, was obtained from Dunner and used for the experiments. 5 types of grain were represented: Australian wheat, Argentine maize, Canadian wheat, English wheat and English barley. The particles

under the microscope showed various characteristics in common but the proportions varied. English wheat, for example, was mostly sharply pointed needles, Australian wheat predominantly flake structures. The particles stain well with Congo red. Chemically the ash of the dust varies in its silica content from 39 gm. to 63 gm. per 100 gm. ash. In the experiments 53 rats were treated by the intratracheal method of KETTLE [*ibid*, 1934, v. 9, 378]; 25 mgm. dust suspended in 0·5 to 1 cc. physiological salt solution was used in each case. Only 19 animals showed pathological changes which could be attributed to the dust. Histologically these changes were in 3 stages.

(1) In animals dying in up to 23 days, there was purulent bronchitis often accompanied by bronchopneumonia which partly resulted in abscesses. Dust particles were definitely identified in the bronchi along with many polymorphonuclear leucocytes.

(2) Lungs of rats dying later showed a characteristic appearance of dilated bronchi filled with necrotic material. The bronchial epithelium was replaced by a granulation tissue, covered by an inner layer of foam cells. A narrow layer of polymorphonuclear leucocytes was found at the margin. Grain particles could not be identified in these bronchiectatic cavities.

(3) Changes, mostly occurring later than the bronchiectatic cavitation took the form of foreign body reaction. Swollen grain particles lay in connective tissue among a great number of giant cells. The animals showing this change survived up to 365 days. No affection of the lymphatic system of the lung was found. No silicotic change or fibrosis was observed.

Some of the lesions produced may be the result of the method of injection used. But of more importance is the particle size which in the grain dust averages 50 to 60 microns. A size of 0·5 up to 5 microns is considered the most important and the large size of the grain particle would prevent them reaching the respiratory bronchioles and alveoli. The silica content of the particles although high, is amorphous and does not produce fibrosis.

The fact that only 19 out of 53 animals showed reaction to dust is probably due to these animals coughing up the dust when recovering from the narcosis used during the operation.

In order to find out if similar results appear with other organic dusts, bagasse dust was used in similar experiments. Similar results were found after 20–80 days but, later, foreign body nodes were found disseminated in the interstitial tissue and in the ends of the respiratory bronchioles. It is suggested that the deeper penetration of the dust is due to the smaller size of bagasse dust which may range in average 2–4 microns. Again no fibrotic change was found. *Charles L. Sutherland*

ONITUKA, M. **[Studies on Experimental Pneumoconiosis produced by Tobacco Dust]** *Igaku Kenkyu*. Fukuoka. 1960, Oct., v. 30, No. 10, 2892–909, 10 figs. [42 refs.] [In Japanese.]

After giving (in the English summary) details of examination of dust in a tobacco factory, clinical examination of workers there, and some experimental work in rats, the author concludes as follows:—

"The above-mentioned study discloses that inhalation of tobacco dust for a long period of time in the tobacco manufacturing factories possibly causes pneumoconiosis under certain conditions, but the general clinical signs and cardio-pulmonary function disturbances caused supposedly by pneumoconiosis are scarcely observed. All the pneumoconiosis-suspects, however, which the author has found out in his X-ray tests, are those who have long worked in the factories since the days of poor equipment. In view of the ever improved facilities of factory and labour conditions together with the health administration, at present and in time to come it seems that there will be rare chances of pneumoconiosis to occur. There is, however, still possibility of improvements of working environment. The workers' personal conditions are a matter of debate as regards the possible disease, so that further care and interest are to be demanded".

ZIELHUIS, R. L. De Industriële Loodintoxicatie in Nederland. Beschouwingen en onderzoekingen. **[Industrial Lead Intoxication in the Netherlands. Observations and Investigations]** pp. viii + 271, illustrated. English summary. 1959. Leiden: Nederlands Instituut voor Praeventieve Geneeskunde.

This is a monograph on all aspects of lead intoxication, particularly in industry in the Netherlands. The first 6 chapters, comprising 103 pages, deal with a general description of lead poisoning, the definition, the pharmacology of lead, and the signs and symptoms. Haemopoietic effects are described in some detail, with special reference to toxic porphyrinuria and the effect upon the marrow and the peripheral blood. An account of the occurrence of lead poisoning in industry is given, and the possibilities of prevention and several prophylactic measures are described.

The next 10 chapters, comprising 132 pages, deal with the author's own observations on lead poisoning in the Netherlands. Chapter 7 is devoted to the analysis of 233 cases out of a total of 242 known cases of lead intoxication to which compensation had been paid by the Social Insurance Bank during 1953–54. There was some doubt as to the authenticity of all the cases, and the author criticizes the criteria used in diagnosis. Lead poisoning is the foremost cause of industrial intoxication in the Netherlands. From 1946 to 1956, 1,050 cases occurred, whereas there were 1,001 cases of carbon monoxide poisoning and 712 cases of poisoning due to benzene and its homologues during the same period. In chapters 8 and 9 new methods of counting basophil punctate erythrocytes are described and discussed, with particular reference to dark-ground illumination. A survey is described in which the variation in the number of reticulocytes and basophil punctate erythrocytes was determined by counting at various times during the same day.

The remaining chapters deal with investigations of exposed workers, long-term investigation of lead workers, the relation between exposure and effect, the investigation of the state of health of workers in different lead-processing industries, the effect of the administration of vitamin B12 on the reaction to lead exposure, and experimental investigations in animals.

The thoroughness with which the author has covered

the field is illustrated by the extent of the bibliography, which occupies 8 pages. *Anne Tothill*

DORDEVIC, S. & STANKOVIC, M. Aerozagadenje i komunalni saturnizam u selu Malo Rudare. [**Aerial Pollution and Communal Saturnism in the Village of Malo Rudare**] *Higijena.* Belgrade. 1960, v. 12, No. 1, 35–44, 1 fig. [13 refs.] French summary.

The authors have investigated the effects of air pollution in the village of Malo Rudare, Yugoslavia, which is situated near a lead and zinc smelting works. The main sources of pollution were sulphur dioxide, dust and lead oxide; the air concentration of sulphur dioxide was 1 mgm., and of total dust 3·4 mgm. per cubic metre respectively. The lead content of the surface layers of the soil ranged from 86 to 220 mgm.%. The air contained 59–136 μgm. of lead per cubic metre (mean 117 μgm.), and the water 23–63 μgm. per litre. Among 107 of the 114 inhabitants investigated 86% suffered from pharyngitis, 70% from enlargement of the tonsils, 62% from conjunctivitis, 33% from rhinitis and 10% from bronchitis; in 78·2% the red cell count lay between 2·5 and 3·5 million. In 71 persons examined the blood contained 37–70 μgm. of lead per 100 cc., with a mean value of 49·3 μgm. The urine contained 56–301 μgm. of lead per litre (mean 136·8 μgm.) and 9·9–109·8 μgm. of coproporhyrin per litre (mean 43·48). *D. J. Bauer*

BARTOLOZZI, O. & ZURLO, N. Effetti della profilassi con versenato di calcio negli operai esposti al piombo. [**Effects of the Preventive Treatment with Calcium Versenate in Workers exposed to Lead**] *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 607–11. English summary.

The authors from the great Clinic of Industrial Medicine at Milan report on the use of Ca versenate in a large accumulator works employing about 400 people. The works, which are shortly to be replaced by a completely modern factory, are nonetheless provided with almost every known means of combating the risk of Pb poisoning, both as regards special apparatus and as regards the employees themselves. In addition, all workers are seen by a doctor at least 4 times a year; blood films and Hb are examined twice a year; urinary coproporphyrin is tested one or more times a year as necessary, and when required samples of blood and urine are sent to the Milan clinic for tests on urinary and blood Pb and protoporphyrin; while in the last 5 years (1955–59) all the workers have had chest X-ray examinations at least 3 times. However, in spite of all these most excellent precautions the risk of Pb poisoning is still present.

The prophylactic value of Ca versenate having previously been tested on 10 persons with good results, all workers were given each year from 1955 onward two cycles of Ca versenate. Each cycle consisted of 2 gm. of the chelant given orally every morning for 10 days, then a 10-day interval followed by another 10 days' treatment. In some workers the complete cycle was repeated. Vitamin B12 and liver and Fe extracts were given after each cycle. The drug was well tolerated, side-effects being minimal and occurring only in the first few days and consisting of very slight abdominal pain.

The results were excellent. The general health of the workers was better than in the company's other factories, and compared with the period 1949–55 when 9 patients were sent to hospital for Pb poisoning, between 1955 and 1959 there was only 1. Several patients were found to have a high urinary Pb but none showed any signs of poisoning.

The authors consider that (1) in view of the fall in urinary coproporphyrin after versenate has been given, any test for this is of no value as an indication of risk; (2) although urinary Pb may be high the absence of any signs of Pb poisoning is noteworthy; (3) finally, the lability of the urinary lead against the daily amount absorbed suggests that the renal threshold for lead may be altered by the chelant, thus opening the way to fresh investigations on its action.

[There is a mistake in the text near the bottom of p. 609 where the table mentioned should be 4 instead of 3.] *W. K. Dunscombe*

SMITH, J. P., SMITH, J. C. & MCCALL, A. J. **Chronic Poisoning from Cadmium Fume.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 287–96, 9 figs. on 4 pls. [24 refs.]

This review, from the Department of Pathology and Occupational Health, University of Manchester, has plates of whole lung sections and slides of trachea, bronchus, lung and testis. It is based on 5 cases [this *Bulletin,* 1954, v. 29, 834; 1956, v. 31, 295; 1958, v. 33, 485; 1959, v. 34, 1025]. Each history and post-mortem is described, and the Cd tissue concentrations in 4 cases and 3 controls. The 5 subjects were exposed to Cd for 32, 9,7,8 and 9 years; the years since the last exposure were respectively 2,5,6,10 and 18; the ratios between Cd concentrations in kidney and liver were respectively 0·18, 0·87, 0·97, 2·15 and 2·5, suggesting movement from liver to kidney as it is unlikely that excretion could account for the differences. High tissue concentrations show that excretion was not rapid. From the lungs, the Cd becomes widely distributed, accumulating especially in liver and kidneys, and also in glandular tissue such as thyroid, pancreas and testis. Significant amounts were found in bile and urine.

Diffuse emphysema was observed with no histological evidence of chronic bronchitis; there was no history of cough with sputum. In 2 cases the sub-pleural zones were not affected. Cd fume—nascent, dry, reactive and of small particle size—has no immediate irritant effect, and high concentrations can be inhaled which damage alveoli. Repeated inhalation of lower concentrations rupture alveolar walls, leading to diffuse emphysema.

No significant histological changes were seen in kidneys, except in 1 case, or in liver, testis or other tissues. There was depression of maturation in 4 testes examined, but plentiful mitotic activity in spermatocytes suggested that this was an effect of terminal illness.

M. Patricia Fitzsimons

DOWNS, W. L., SCOTT, J. K., STEADMAN, L. T. & MAYNARD, E. A. **Acute and Sub-Acute Toxicity Studies of Thallium Compounds.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 399–406, 3 figs. [13 refs.]

Thallium acetate (TA) in aqueous solutions and a suspension of the oxide (TO) were administered intraperitoneally, orally and intravenously to compare lethal ranges and LD50. Lowest single lethal doses in mgm. Tl per kgm. in rabbits, rats and guineapigs respectively were: intraperitoneally as TA 13, 20, 7 and as TO 60, 92, 30; orally as TA 19, 29, 12 and as TO 30, 20, 5 and in dogs as TA 20 and as TO 30; in rabbits intravenously as TA 20 and as TO 39. In female rats the single 7-day LD50 were: intraperitoneally 23 mgm. Tl per kgm. for TA and 72 for TO; orally 32 and 39.

Ingestion studies on weanling rats—after preliminary tests with diets containing up to 0·5% TA or 0·05% TO —were carried out for periods up to 15 weeks on diets containing up to 0·005% of either compound. Tables and figures show cumulative mortality and growth rates. As little as 0·003% caused marked growth depression in 30 days; higher concentrations were fatal, and some animals died later on 0·003%. Depilation started in 2 weeks on 0·0015% TA and was marked in 4 weeks on 0·002% TO. The skin showed total atrophy of follicles, thickening of collagen bundles causing pressure, hyperactivity and involution of sebaceous glands with excess fat and keratinous degeneration; there was depletion of Ca or Mg ash or of both. Other organs and tissues were normal, except for increase in kidney weights.

Spectrochemical analyses of tissues showed the kidney to be the principal site of deposition. In rats fed 0·003% TA for 63 days or TO for 106 days the amount of Tl as μgm. per gm. organ wet weight were respectively: kidney 24 and 31, liver 16 and 13, bone 19 and 0, with small amounts in spleen, lungs and brain.

M. Patricia Fitzsimons

RINEHART, W. E. **Studies on the Toxicity of Triethylborane (TEB).** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 389–93. [12 refs.]

These acute toxicity tests with TEB and its combustion products suggest that exposure to the uncombusted vapour should be kept to a minimum. $(C_2H_5)_3B$ is a clear colourless liquid; BP 95° C. The vapour pressure at room temperature is approximately 50 mm. Hg. Vapours in air will ignite spontaneously at partial pressures of approximately 1 mm.Hg. (1,300 p.p.m.). For inhalation studies dry N was bubbled through 8·9% TEB in mineral oil and the TEB-N vapour mixture was diluted with air. For exposures to combustion products, N was bubbled through TEB and the vapours were directed through an aluminium tube to the burning chamber where they ignited spontaneously. For oral tests the 8·9% oil solution, 77·9 mgm. TEB per ml., was administered intragastrically, and a 12·4% oil solution, 106 mgm. TEB per ml., was injected intraperitoneally. The rats that died during the 7-day observation period were included in toxicity data calculations. There were no deaths from inhalation of the combusted vapours, 177 and 300 p.p.m., for 4 hours, or 580 and 785 p.p.m. for 60 and 30 minutes respectively, or toxic signs except loss of weight from dehydration caused by heat.

The 4-hour LC50 was 700 p.p.m.; concentrations of TEB were 589–760 p.p.m. The oral and intraperitoneal LD50 were 235 and 22·7 mgm. per kgm. respectively. By all routes TEB caused convulsions and inhalation caused also respiratory irritation, with blood-stained fluid in the lungs of rats which died. Death occurred soon after administration of TEB and also during inhalation. Survivors mostly regained weight. Convulsions were not always fatal.

On the basis of boron content TEB, a strong reducing agent, was more toxic than decaborane. The oral and intraperitoneal LD50 of TEB were 25·8 and 2·5 mgm. B per kgm., and the LC50 was 0·31 mgm. B per litre; for decaborane these data were 57 and 20·7 mgm. B per kgm. and less than 0·42 mgm. B per litre.

M. Patricia Fitzsimons

GABOR, Sylvia & RAUCHER, K. Studien zur Bestimmung der zulässigen Benzol- und Monochlorbenzol-Grenzkonzentrationen. **[Studies of the Admissible Benzene and Monochlorobenzene Basic Concentrations]** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 223–31, 4 figs. [11 refs.]

The clinical picture of "pre-" or "latent" benzene poisoning has been said to be characterized by transient symptoms of headache, giddiness, drowsiness, irritability, loss of weight, loss of appetite and slight anaemia, and it is stated that these may follow constant exposure to concentrations of 0·03 to 0·19 mgm. per litre.

In Rumania the "normal" concentrations of benzene and monochlorobenzene in factories are agreed at 0·1 and 0·05 mgm./litre respectively. The authors have carried out an investigation to confirm the actual existence of these limits and to discover whether they cause any functional disturbances which would permit an early diagnosis of intoxication.

This included estimations of the concentrations in a factory producing DDT, a clinical study of the workers, a chronaximetric test, analysis of certain enzymes of the blood and experimental poisoning of animals by benzene and monochlorobenzene.

The air concentration of both substances remained constant over a period of 3 years at 0·0005 to 0·15 mgm./litre for benzene and 0·0005 to 0·35 for monochlorobenzene. Chloraldehyde, sulphur dioxide and chlorine were also present, but in amounts varying from time to time with technical variations, the highest concentration (0·001 to 1·8 mgm./litre) being that of sulphur dioxide.

Chronaximetric tests of the extensor tibialis of white rats exposed to 0·1 mgm./litre of benzene and monochlorobenzene for 3 hours every 2 days indicated a disturbance of the nervous system between the 7th and 14th week. Monochlorobenzene caused a more prolonged inhibition at a lower level than benzene. Alimentary conditioned motor reflexes were also more strongly inhibited by monochlorobenzene.

Alterations in activity of certain enzymes—leucocytic

peroxidase, indophenol oxidase and carbon dioxide anhydrase—appeared earlier than those of the nervous system and were irreversible after 37 weeks.

Haematological disturbances in the workers (a tendency to slight leucopenia) were much later in appearance—only towards the end of the third year. The authors believe that 3 years is too short a time, in the existing conditions, to reveal the classical symptoms of chronic benzene poisoning, and that even when the concentrations of benzene and monochlorobenzene are kept to the "normal" level the combined effect of other toxic substances present must be considered.

It is concluded that nervous disturbances may appear immediately upon exposure without other symptoms ascribable to intoxication, and that concentrations of 0·1 mgm./litre for benzene and 0·05 mgm./litre for monochlorobenzene should be considered the maximum limits for avoidance of rapid severe injury to health.

Ethel Browning

HENSON, E. V. **The Toxicology of some Aliphatic Alcohols. Part I.** *J. Occup. Med.* Chicago. 1960, Sept., v. 2, No. 9, 442–6. [15 refs.] **Part II.** *Ibid.*, Oct., No. 10, 497–502. [37 refs.]

In this most useful review the toxicities of the shorter chain aliphatic alcohols are compared and in the second part the actions of 4 are described. Nomenclature of the series is illustrated by the 8 isomers of amyl alcohol: each is given its formula and 3 synonyms according to common, carbinol and Geneva terminologies.

By some measurements the intensity of anaesthetic-narcotic action increases with chain length and decreases, relatively, with branching and secondary and tertiary positions of the hydroxy radicle. Alcohols are irritating to mucous membranes and vapour concentrations which can be tolerated decrease in the series from C_3 to C_9. Oral tests in rats show toxicity increasing up to C_4 or C_5 and then decreasing. Phagocyte inhibition increases up to C_7 by a factor of 3 based on molar concentrations. Alcohols can be excreted unchanged or primary alcohols oxidized to the aldehyde and then to the fatty acid, secondary alcohols to ketones or conjugated with glycuronic acid, tertiary alcohols as glucuronides. Alcohol when unspecified means ethyl alcohol.

Methanol and ethanol, the causes of much morbidity, though not now from industrial use, are considered in detail. Methanol poisoning usually follows ingestion of adulterated or denatured alcohol though symptoms have followed skin absorption or inhalation of 300 p.p.m. The narcotic dose is 10 gm. per kgm. Treatment aims at preventing stage 2. Slight, possibly temporary inebriation is followed 6–24 hours later by acidosis from metabolites and probably secondary enzyme inhibition. Stage 3 is nervous system degeneration with optic nerve and retinal destruction and basal ganglion necrosis. Methanol is distributed rapidly, a small proportion is excreted, the rest is slowly oxidized to toxic metabolites by alcohol dehydrogenase in liver and kidney unless ethanol is also present. Ethanol is preferentially oxidized by the same enzyme—hence the specific treatment with this alcohol until the methanol can be excreted unchanged. Ethanol can be absorbed through the skin with insignificant effect but prolonged inhalation can cause symptoms. Blood concentration of 550 mgm. per 100 cc. which results from 3 gm. per kgm. is usually fatal. It is metabolized at a rate of 200 mgm. per kgm. per hour.

Isopropanol has displaced ethanol for many industrial purposes. Intoxication has followed its use in liniments, possibly because inhaled. It is rapidly distributed and slowly oxidized in the liver to acetone which also is narcotic. The LD50 of acetone is 9·75 gm. per kgm., of isopropanol 10·7 and of ethanol 21·3. However, blood levels show that isopropyl is 3 times as narcotic as ethyl alcohol.

Butanol is a solvent for resins, varnishes and lacquers. It is absorbed rapidly from lung and intestine and oxidized completely. The LD50 of this more powerful narcotic is 4·3 gm. per kgm. Nevertheless, solutions have been given intramuscularly and intravenously to stop bleeding and pain without ill effect. The vapour has caused conjunctivitis from 50 p.p.m., and also keratitis.

M. Patricia Fitzsimons

BOCQUET, P., CHARY, R. & JAYOT, J. Toxicité percutanée de l'acide cyanhdrique. **[Percutaneous Toxicity of Hydrocyanic Acid]** *Arch. Malad. Professionnelles.* Paris. 1960, July–Aug., v. 21, Nos. 7/8, 456–8.

Quantitative determinations were made of HCN toxicity by skin absorption in guineapigs and also in rats; evaporation of the liquid and inhalation of the vapour were prevented. In 21 rats, of about 150 gm., tail immersion tests gave absorptive surfaces of about 8–9 cm² in test tubes filled to a height of 10 cm. with chilled HCN. Death took 10–70 minutes, mean 33.

A small polythene cup, the open end of which was about 3 cm², was stuck to the shaved, abdominal skin of the guineapigs, and through a hole pierced in its base, various doses of HCN were injected by syringe. The mortality rates in 57 animals, of 450–500 gm. are shown below:

Temperature	Dose mm³ HCN	Mortality Rates	Time of Death
25°C.	500	5/5	10–14 minutes
„	300	5/5	15 „
„	200	7/7	21–28 „
„	100	5/10	15–22 „
15°C.	90	9/10	10–20 „
„	50	5/10	38 „
„	30	1/10	240 „

A dose of 30–50 mm³ (20–35 mgm.) was capable of killing a guineapig weighing 1 lb. by skin absorption. The skin LD50 was about 100 mgm. per kgm. body weight per surface of 3 cm², a small amount when considering how men may be splashed at work and clothing soaked. Cooling—which would imply delayed evaporation—increased the skin toxicity. At work, not only masks and gloves, but also full protective clothing is necessary, including an impermeable hood for head and neck.

M. Patricia Fitzsimons

RAYMOND, V. Les intoxications des puisatiers. **[Occupational Poisonings in Workers in Well Boring]** *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 517–23.

In this paper the author draws attention to his experience that poisonings by atmospheric constituents of workers in wells are relatively frequent. 19 such poisonings have been observed in the last few years and among these there were 10 deaths.

Short case reports of 15 poisonings are given. There are 3 groups of causes:—(1) gases derived from the soil mainly carbon dioxide, carbon monoxide and other volatile substances such as sulphuretted hydrogen, (2) gases from petrol driven motor pumps which are replacing hand pumps—such as CO, CO_2, SO_2, nitrous fumes, hydrocarbons and others and (3) gases such as CO and nitrous gases and fine dusts from blasting operations.

There is a discussion of these 3 causes and a list of the preventive measures which should be taken.

M. E. Delafield

GODARD, J., THOMAS, C. & DELABROISE, A. Réflexions à propos de quelques séquelles graves d'intoxication oxycarbonée. **[Thoughts about Some Serious After-Effects of Carbon Monoxide Poisoning]** *Arch. Malad. Professionnelles.* Paris. 1960, July–Aug., v. 21, Nos. 7/8, 479–81.

Mainly to draw the attention of lay people in industry to the possible after-effects of CO poisoning, an account is given of 3 blast furnace workers who, with others, were overcome by CO in separate accidents. All 3 reacted differently from the other victims who apparently recovered from unconsciousness quickly and completely, and all 3 had permanent brain damage. Their previous histories, well known to the industrial medical officers, had certain things in common: for many years they had worked where there was a risk of exposure to CO, they had been poisoned before and at the time of the accidents they were healthy, alert men; one, aged 55, though he had been an alcoholic, was normal for his age. This man sounded the alarm when his companions lost consciousness and then fell but remained conscious. When he left hospital there was still some CO in the blood, and he had tremor, more marked on one side. This persisted, he developed parkinsonism and remained psychically below normal. The other 2, aged 28 and 38, remained unconscious for some time, with agitation or convulsions and abnormal reflexes. The older man, who took some 3 weeks to come out of his coma, was left with amnesia, disorientation, diminished vocabulary, mental incapacity, disordered movements and other signs of cerebral atrophy. The younger developed aggressive behaviour, headaches and right-sided blindness. No other cause was found for their condition.

CO poisoning, properly treated, even slight in degree, may lead to serious sequelae. Coma with shaking and abnormal reflexes is of grave import. Previous minor attacks may be an aggravating element. A subacute attack in an older subject may precipitate latent disease. All cases, however slight, should be reported to safeguard the patient's future. Persisting headache, apathy, behaviour changes, giddiness and abnormal skin sensations justify a neurological and psychiatric examination.

M. Patricia Fitzsimons

JONES, A. T. **Fatal Gassing in an Acetylene Manufacturing Plant.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 417–22, 3 figs.

This accident happened before the similar one attributed to chronic phosphine poisoning was published [this *Bulletin*, 1959, v. 34, 463]. The night operator, aged 24, previously healthy, was found lying across an opened generator calcium carbide feed hopper with his head inside. He had been alone for 2 hours. The hopper was almost empty. The post mortem showed parchment abrasions on the chest, wet abraded areas like burns on the face, oedematous upper eyelids, singed eyebrows and hair, pulmonary congestion and oedema with recent haemorrhage. scattered coronary atheroma but no infarct, and 8% carboxyhaemoglobin in the blood. No explosion had occurred.

The duty of ensuring continuous enclosed acetylene production by keeping the hoppers adequately filled involved nevertheless removing the hopper lid periodically to inspect the level of carbide. To do this the operator had to lean over the hopper, which was 2 feet above floor level, in such a way that, if overcome, he would be held in that position with his head over the opening. Inspections would mean exposure to hopper gas for about 1–1½ hours per shift. The carbide specification provided a raw gas with a minimum of 99% acetylene and maxima of 0·15% H_2S, 0·06% phosphine, 0·001% arsine and 0·1% NH_3. The puff of gas which escaped under pressure when the hopper lid was loosened contained 1% acetylene at breathing level, too low a concentration of any impurities to cause initial collapse. Tests for CO in the hopper gas were inconclusive: CO could have been adsorbed on carbide during manufacture and released during the water-carbide reaction. In the hoppers O_2 ranged from 8 to 20%. Experiments showed that sufficient temperature developed with deposited carbide dust and skin moisture to cause burns and singed hair.

Illuminated glass ports in the hoppers have now been found practical for inspection. Compressed air respirators were used temporarily and radioactive indicators were considered.

M. Patricia Fitzsimons

WEEKS, M. H., DOWNING, T. O., MUSSELMAN, N. P., CARSON, T. R. & GROFF, W. A. **The Effects of Continuous Exposure of Animals to Ethanolamine Vapor.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 374–81, 1 fig. [23 refs.]

Monoethanolamine (MEA), used in air purification processes for removing CO_2 and similar gases from exhausts, could be carried into the air stream. The apparatus is illustrated in which volatilization was effected from 30% aqueous MEA at the U.S. Army Chemical Centre.

Dogs, guineapigs and rats were exposed without break

to 102, 75 and 66 p.p.m. for 30, 24 and 30 days respectively, or for 90 days to 26, 15 and 12 p.p.m., and other dogs to 12 p.p.m. Younger rats and dogs were exposed to 5 and 6 p.p.m. for 40 and 60 days. The dominant effects were skin irritation and lethargy. At high concentrations dogs died after 25 or 30 days, 75% of 22 guineapigs between 10 and 24 days, and 83% of 45 rats between 14 and 28. Increased activity was quickly followed by depression. Skin became wet from the condensed alkali, ulcerated and necrotic. Rats' hair became thin and guineapigs' loosened; follicles showed no reasons for this. In dogs, leg tremors began after 70 hours and increased. Râles and fever lasted 2 weeks. Turbinate erosion, lung inflammation and liver and kidney damage were found and changes in intestine, spleen and testes. Blood albumin decreased and globulin increased. There was anaemia and leucocytosis. Blood chemistry and other tissues were normal and so was rodents' blood. At intermediate concentrations signs were similar but less severe. At low concentrations decreased activity began after 2–3 weeks; some dogs lost weight; rodents' rate of growth was similar to controls. Physical, pathological and biochemical examinations were normal, except in skin microscopy.

It was calculated from the rat 12 p.p.m. exposure that by continuous inhalation MEA was at least 10 times as toxic as by ingestion. It was detected at 2·6 p.p.m. by some volunteers by sensation rather than odour. The narcotic effect could be dangerous. For continuous exposure, concentrations should be below 5 p.p.m.

M. Patricia Fitzsimons

CLAYTON, J. W., Jr., DELAPLANE, M. A. & HOOD, D. B. **Toxicity Studies with Octafluorocyclobutane.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 382–8, 5 figs.

This "food propellant," a gas at room temperatures, had to be tested by repeated inhalation to determine its safety in food, instead of by feeding experiments. Rats, mice, rabbits and dogs, after preliminary tests, were exposed to 10% octafluorocyclobutane (OFCB) in air at least 90 times for 6 hours each day on 5 days each week. A photograph shows the exposure chamber designed to take 4 dogs—separated by partitions—and 20 small animal cages, and also to conserve the limited supply of food grade OFCB. Preliminary tests showed no symptoms, pathological or microscopic changes in rats exposed for 4 hours to 80% OFCB in O_2, nor any anaesthetic response in mice rotated for 10 minutes in this mixture—except transient effects on respiration. There were no immediate or delayed deaths.

Growth responses, serial urine examinations and blood counts, organ weights and, in the dogs, serial blood pressures and heart rates were normal except for slight effects considered insignificant, as follows. The heart rate of 1 of 2 dogs which fought each other frequently increased during the experiment; red blood cell counts tended to be lower and haemoglobin concentrations to be higher during exposure than before. Average white cell counts in female rats were lower than controls. All controls (no dogs) were exposed in the test chamber under similar conditions of O_2 and CO_2 control. Serial estimations were made of blood sugar, N, cholinesterol, cholinesterase, alkaline phosphatase and bromsulphthalein retention. Microscopy of all tissues including, *e.g.*, thyroid and eye, was normal.

No harmful effects were found after single or repeated inhalation of concentrations far higher than would be met in routine use. It is concluded that OFCB is a safe propellant for food products.

M. Patricia Fitzsimons

MASTROMATTEO, E., FISHER, A. M., CHRISTIE, H. & DANZIGER, H. **Acute Inhalation Toxicity of Vinyl Chloride to Laboratory Animals.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 394–8. [10 refs.]

After 2 accidental deaths in a plant engaged on polymerization of the gaseous monomer [this *Bulletin*, 1960, v. 35, 765] groups of 5 mice, 5 rats and 5 guineapigs were closely observed during exposure to 10, 20 or 30% vinyl chloride in air for 30 minutes. Guineapigs, the most resistant, were exposed to 40% for 30 minutes; 1 died during exposure, 1 died later and 3 survived and took 30 minutes to recover from narcosis. At 10% irritation was followed by increased activity in 5 minutes, tremor and incoordination in 10, and in mice and rats narcosis in 25; on removal 1 guineapig was unconscious; the animals recovered in 5 minutes. At 20% narcosis developed in 15 minutes, and in mice and rats frothing at mouth and nostrils appeared in 25 minutes; 1 mouse then stopped breathing. At 30% these signs appeared in 5 minutes, mice stopped breathing in 10 and rats in 15 minutes; 1 guineapig died after removal within 24 hours. In the dead animals the principal changes were congestion in lungs, liver and kidneys and, from the higher concentrations, severe damage to tracheal epithelium and pulmonary oedema and haemorrhage. The liver of the guineapig which died after 30% showed severe fatty degeneration of the liver. The blood of animals which died during exposure had a tendency to remain unclotted. Minimal degeneration of renal tubular epithelium was noted in the mouse which died during 20% exposure and also in another which was killed, as were all survivors, 14 days after the exposures. Changes suggesting fatty infiltration of the liver in some animals were not confirmed in frozen section stained by Sudan III. Survivors showed little difference from controls except pulmonary congestion.

M. Patricia Fitzsimons

CRISMER, R., MIGNOLET, F., RONDIA, D. & HEUSGHEM, C. Toxicité des huiles incombustibles. **[Toxicity of Incombustible Oils]** *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 531–3.

The so-called incombustible oils are used for various purposes in industry. The composition of these varies according to need but they contain organic phosphates which are described. Their toxicity is attributable to the presence of tri-ortho-cresyl phosphate.

Here recorded is a case of poisoning in a man who was exposed to droplets of the oil from open gears, in a machine for transmitting power to a revolving fan. There

is a clinical description of the symptoms, signs and results of examination which were those of a relatively slight case of organic phosphate poisoning from which the man recovered.

There is very slight risk to health from the use of these oils in industry provided they are in a closed circuit and the workers know the risks of exposure.

M. E. Delafield

BALDI, A. Controllo del tasso del colesterolo totale dei lavoratori di una raffineria di petrolio. **[Control of the Total Cholesterol Rate in Workers of an Oil Refinery]** *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 593–9, 8 graphs. [13 refs.]

The English summary appended to the paper is as follows:—

"The total cholesterol serum was determined on 1,000 workers of an oil refinery during the customary follow-up visits. The values found have been examined on the whole and for individual groups according to age, weight, blood pressure, category, length of shifts, tasks and length of exposure. The figures reported and the graphs plotted have not evidenced any change of the total cholesterolemia of occupational nature."

ROBIN, M. J. Allergie respiratoire professionnelle aux antibiotiques chez des infirmières. **[Occupational Respiratory Allergy to Antibiotics in Nurses]** *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 558–60.

This short paper contains 2 case reports (and reference to a third) of occupational respiratory allergy in nurses which are presented because the author considers that such cases may not be exceptional although there are few references in the literature.

The past history of these nurses is recorded in some detail to indicate how they may have become sensitized to an antibiotic which was penicillin in 1 instance and streptomycin in the other. In both these women the first manifestations of allergy were mainly cutaneous but some years later respiratory symptoms of spasmodic cough and asthma occurred on exposure to the antibiotic. The results of cutaneous tests with the antibiotics confirmed the specific diagnosis. *M. E. Delafield*

SCHILLINGER, J. I. Hygienische Wertung von landwirtschaftlichen Erzeugnissen, angebaut unter Anwendung von Herbiziden. **[Hygienic Evaluation of Agricultural Production with the Use of Herbicides]** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 243–52. [14 refs.]

Compounds recently introduced as weed killers are the sodium salt and the butyl ether of 2,4-dichlorophenoxyacetic acid. These are sprayed in amounts of 100 to 120 litres of a 0·2 to 1·0% solution per hectare by aeroplane and 300 to 600 litres per hectare by land machine, a proportion of 0·75 to 1·0 kgm. of the sodium salt and 0·2 to 0·5 kgm. of the butyl ether.

The author has previously estimated the oral LD50 for rats as 2,000 mgm. per kgm. body weight for the sodium salt, and 1·5 gm. per kgm. for rats and 0·55 gm. per kgm. for mice for the butyl ether, either pure or as an emulsion with the mono- or di-alkylphenyl ether of polyethylene glycols. The toxic effects in rats were drowsiness, roughening of the fur, and within 3½ hours semi-consciouness; when roused they showed poor co-ordination, and oozing of serum at the corners of the eyes followed by drying and crusting. Some died 15 to 20 hours after administration. The butyl ether was much more toxic than the sodium salt. In the present investigation sub-toxic doses (about one-quarter of the LD50) were given daily by mouth to rats—0·375 gm. per kgm. of the pure preparation of the butyl ether in the form of an emulsion. Some died, or were killed at the end of one or one and a half months, having ingested 2·4 to 4·2 gm. A few animals showed a decrease in the haemoglobin level, and a later disappearance of eosinophils and an increase in granulocytes; a diminution of activity of blood catalase and peroxidase and a fall in blood protein. Some animals showed an increase of gamma globulin, and many a shrinkage of testes and prostate with injury of spermatogenesis, fatty changes in the liver and degenerative changes in the renal tubules. Sub-toxic doses of the sodium salt (500 mgm. per kgm.) showed similar liver and kidney changes, decrease in haemoglobin and erythrocytes and catalase activity, but no disturbance of spermatogenesis.

An experiment of longer duration (10 to 12 months) showed no cumulative effect of either preparation.

The long-term effect of an oat harvest from fields treated with a double dose of both herbicides was tested on rats, rabbits and mice, estimations being made of the prothrombin time, ferment activity and plasma albumin. Urine analyses were made twice during the investigation, and after the animals were killed the liver was examined for fat and lipoid phosphorus content. None showed any difference from the control animals. Mice fed on oats grown on fields treated with the sodium salt for 1 generation and with the butyl ether for 5 generations showed no disturbance of fertility, no alteration in the weight of the young and no histological abnormality of the internal organs.

It is concluded that both the sodium salt and the butyl ether of dichlorophenoxyacetic acid can be safely used as weed killer in a dosage not exceeding 2·0 kgm. per hectare of the sodium salt and 0·8 kgm. per hectare of the butyl ether. *Ethel Browning*

BILLEWICZ-STANKEIWICZ, J. & PAWŁOWSKI, L. Experimentelle Untersuchungen über den Einfluss des Kalkstickstoffes auf die höhere Nerventätigkeit der Tiere. **[Animal Experiments on the Influence of Nitro-Chalk on the Higher Nerve Centres]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Sept., v. 6, No. 9, 540–49, 2 figs.

Nitro-chalk (*Kalkstickstoff*) is an artificial fertilizer which consists mainly of calcium cyanamide with small

amounts of calcium oxide, carbon and other additions. It has been reported that workers engaged in distributing this fertilizer on the land suffer from transitory symptoms, chiefly lassitude, shivering, difficulty in breathing, a feeling of heat, erythema, vomiting and diarrhoea.

This toxic effect was investigated in rats and the methods employed and the results obtained are fully described in this paper. The method was one which has been used by other workers in pharmacological and toxicological testing. It consists of observing the effect of the test substance on animals (rats in the present work) in which conditioned reflexes have been induced. The stimuli applied to the animals in conditioning were the sound of a bell, light and a humming noise.

The animals were then exposed to measured amounts of the fertilizer in dust form in an inhalation chamber for various periods of time. The main finding was that inhalation of 2·9 mgm. (2·3 million particles) of the dust per litre of air for a period of 1–2 hours caused first a weakening and then the disappearance of many of the positive reflex reactions. This phenomenon lasted for 10–19 hours after the end of the inhalation period and the conditioned reflexes only returned to normal during the succeeding 11 days. *M. E. Delafield*

BLABER, L. C. & CREASEY, N. H. **The Mode of Recovery of Cholinesterase Activity *in vivo* after Organophosphorus Poisoning. 1. Erythrocyte Cholinesterase.** *Biochem. J.* 1960, Dec., v. 77, No. 3, 591–6, 5 figs. [24 refs.] **2. Brain Cholinesterase.** *Ibid.*, 597–604, 6 figs. [11 refs.]

SASSI, C. & CAVAZZUTI, F. Metabolismo lipidico del fegato nella intossicazione sperimentale acuta e subacuta da insetticidi fosforati. **[Lipid Metabolism of the Liver in Experimental Acute and Subacute TEPP and Parathion Poisoning]** *Med. d. Lavoro.* 1960, Aug.–Sept., v. 51, Nos. 8/9, 553–9, 2 figs. [19 refs.] English summary.

After summarizing the action of the organic phosphorous compounds on the various esterases, the authors point out that the toxic action of such compounds may cause organic changes unrelated to any direct effect on cholinesterase, especially in the case of subacute and chronic poisoning with the rather less toxic products now in use, the lesions then being masked by the predominating nervous symptomatology.

As many of these organic changes affect the liver and because the hepatocytes are of extreme importance in lipid metabolism, the authors carried out experiments on adult white rats of each sex with acute and subacute poisoning by TEPP and parathion, and determined the total lipids, phospholipids, neutral fats and fatty acids, in the liver. Both drugs were given intramuscularly, dissolved in olive oil, as follows:—TEPP acute 0·8, subacute 0·16 mgm./kgm.; parathion 5, and 1 mgm./kgm. respectively.

The animals were divided into 5 lots as follows: (1) 7 controls; (2) 4 given one acute dose of TEPP and killed 48 hours later; (3) 10 given subacute doses of TEPP for 14 days and then killed; (4) 4 given one acute dose of parathion and killed 48 hours later; (5) 10 [shown in a table as 6] given subacute doses of parathion for 14 days and then killed. The results were as follows. Both acute and subacute TEPP and acute parathion were well tolerated, but subacute parathion caused death in 4 out of 10, the survivors going off their food and showing staring coats. Tests of the brain cholinesterase in half the animals showed marked inhibition of the enzyme. In the liver after acute poisoning there was very little change from normal, but both subacute TEPP and parathion caused a considerable rise in total lipids and in neutral and acid fats. The animals in lot 5 showed considerable loss of body weight.

The authors consider that blocking of the cholinesterases is not sufficient to explain the changes observed in lipid metabolism as these enzymes are not known to have a direct effect on fat metabolism; a more likely explanation would be a blocking of oxidizing-reducing enzymes or inhibition of the liver carboxylases, but it would seem more logical to relate the changes in lipids to inhibition of the carboxylesterases which are known to be affected by phosphorus insecticides. The more toxic effect of parathion is related to its longer action.

While stating that their experiments should be confirmed the authors point out that any long exposure to even the so-called reduced-toxicity organic phosphorus compounds may cause irreversible changes in the internal organs. *W. K. Dunscombe*

GRIGOROWA, R. Über die Gesundheitsgefährdung durch Wofatox (Dimethyl-p-Nitrophenylthiophosphat) bei der Herstellung eines Schädlingsbekämpfungsmittels. **[Health Dangers of Wofatox (Dimethyl-p-Nitrophenylthiophosphate) during the Manufacture of a Pesticide]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Sept., v. 6, No. 9, 556–60. [15 refs]

Wofatox (dimethyl-p-nitrophenylthiophosphate) is the chief constituent of the pesticide Wofatox-dust, the manufacture and packing of which is described in this paper. Many of the workers in this industry complain of the effects of the inhalation of the dust on their health. Medical examination of the workers showed that in the winter months out of 47 workers 18 (38·3%) and in the summer months out of 35 workers 29 (82·9%) had symptoms of loss of appetite, abdominal pains, disturbances of sight and sleep, lassitude, nervousness and headache. These symptoms were slight in winter but were much worse in summer than in winter.

Cholinesterase activity in plasma was determined in a considerable number of the workers by a method which is described in detail. It was found that this activity was reduced in the summer months for in 27 out of 29 workers the inhibition of activity of cholinesterase was between 11% and 68·4%. These findings are discussed with reference to the literature on other organic phosphates.

There is a short account of the measures which are recommended to be taken for the protection of the workers. *M. E. Delafield*

BRITISH MED. J. 1960, July 16, 215–16: LANCET. 1960, July 23, 201–2. **Poisoning from Organo-Phosphorus Compounds used in Agriculture and Horticulture.**

This warning note on poisoning from organophosphorus compounds was prepared by a panel of experts, and was published at the request of the Ministry of Health. It gives in brief the essential information on the pharmacology, toxic effects, treatment and diagnosis of poisoning with parathion and the many other compounds which depress cholinesterase activity and which are largely absorbed through the skin. Much of this information is contained in the paper on *Toxicity of Pesticides*, by J. M. BARNES, published in this *Bulletin*, 1959, v. 34, 1205–1219, but the present note also contains a list of organizations which supply P2S (used in treatment), with their addresses and telephone numbers, and there is also a list of laboratories at which blood cholinesterase estimations are carried out, and instructions on despatch of blood.

This is a very useful statement, in which the seriousness of poisoning by these chemicals is clearly indicated. The importance of early treatment with atropine and artificial respiration is stressed. The cholinesterase reactivators P2S and P2-AM are important, and they should be given as soon as possible, but atropine injection should never be delayed until these reactivators are available; it should be given at once. *Charles Wilcocks*

FUNCKES, A. J. **Treatment of Severe Parathion Poisoning with 2-Pyridine Aldoxine Methiodide (2-PAM). Report of a Case.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 404–6.

A flagman, aged 29, became dizzy and vomited on arrival at the home airstrip after 4 hours' loading 2% parathion dust for aerial crop dusting. When found semi-collapsed 30 minutes later, he was given 1·2 mgm. atropine. Exposure was not considered great. He had however, worked as a loader during 5 summer months and was known to disregard safety precautions and to be careless in personal hygiene. The odour of parathion was noticed on his clothing after another 30 minutes on arrival at the surgery. He had pin-point pupils and was sweating. Atropine, 0·8 mgm., was injected intramuscularly. In hospital, 3 hours after the first symptoms, a bath was given and 2 mgm. atropine intramuscularly. Additional signs developed: salivation, moist respiration, clonic convulsions, incontinence, disorientation, irregular pulse at 140, and blood pressure 220/110. Intravenous atropine, 2 mgm., was given. Intravenous infusion of 2–PAM [P2–AM] was started 2 hours after arrival at hospital: 1 gm. of 2–PAM in 20 ml. saline was added to 500 ml. of 0·2% saline. Part was injected rapidly for 5 minutes and within another 5 minutes dramatic improvement was noted, when one-third had been given; the remainder was given in 35 minutes. Bladder control was not complete for 8 hours. Intravenous atropine was repeated and was followed by 0·4 mgm. hourly for 8 hours and then every 4 hours for 2 days.

Urinary excretion of paranitrophenol reached 108 μgm. per hour 27 hours after the 2–PAM and was 47 after 54 hours. On the 3rd day 5 alcohol washes of hands and body produced 12 to 70 μgm. of parathion. The red cell cholinesterase was higher than expected in comparison with the degree of illness and with plasma cholinesterase, which indicated that acetylcholinesterase, found in the red cells, was reactivated by 2–PAM. The patient was asymtomatic when discharged 5 days after exposure, his cholinesterase values were rising and a week later they were normal. [Note apparent delay in removing clothing and washing skin.]

M. Patricia Fitzsimons

CHRISTOFANO, E. & HARRIS, W. B. **The Industrial Hygiene of Uranium Refining.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 438–60, 16 figs.

Since 1940, uranium production has steadily increased. U.S. purchases of raw material amount to about 30,000 tons of metal per year. The processes by which the uranium is obtained in the required forms are multiple, elaborate and, unless carefully watched, dangerous to the employees.

The authors take the reader over the ground covered since about 1948, watch being kept by the Health and Safety Laboratory (HASL) acting in concert with the Atomic Energy Commission. In 1948 the University of Rochester (U.S.A.) published the results of an investigation upon rats of the toxicity of uranium. It affects the kidney primarily, the only dangerous mode of entry into the body being *via* the lungs. The quantitative recommendations they made were adopted in the general measures of safety by HASL. The reader is taken seriatim, assisted by graphs and photographs of the working conditions through all of the main processes in these elaborate efforts at obtaining the pure uranium. Whereas many years ago radium was the minute fragment gained by getting rid of the uranium, things have now come full-circle, for radium is a tiresome by-product, very difficult indeed to get rid of. To obtain, however, it is still necessary to pay the cost of an expensive extraction.

The authors' style is at times a little obscure; for instance: "Sampling of uranium-bearing (feed) raw material is carried out to determine an assay on which quality control procedures, accountability requirements and purchase price may be based." In the text there is frequent reference to radon gas, a redundancy since radon is a gas unless one is concerned with liquid air temperatures. We learn that the number of refinery operating personnel has risen from about 400 in 1948 to about 3,000 in 1960. One can gauge the success of continuous efforts at eliminating the air-dust dangers of this kind of work by the following statement: "By 1948 and 1949 men were exposed to as much as 400 times the present acceptable levels; by 1955 the maximum occupational exposure was reduced to 4 times the admittedly conservative permissible level of 110 d/min/cu. m."

S. Russ

HEATING, LIGHTING AND VENTILATION

ANN. OCCUP. HYG. London. 1960, Sept., v. 2, No. 3, 167–227, 19 figs. (2 on pl.). [Numerous refs.]
Heating, Ventilating and Air Conditioning.

A satisfactory environment in which to live and work is an essential requirement, but it is less easy to state what satisfaction means. When it is remembered that uncomfortable conditions can lead to a significant fall-off in work output, or an increase in mistakes, or even in severe conditions to collapse and death, it is somewhat surprising to find how very little is really known about the relationship between a human being and his environment.

The work of BEDFORD and his colleagues in Britain, and of HERRINGTON, YAGLOU and others in America, many years ago laid the foundations of the study by investigating thermal interchange between the body and its surroundings. Dr. T. BEDFORD'S paper in this collection, (*Requirements for satisfactory heating and ventilation,* pp. 167–175) presents a concise summary of the effects of various factors upon the feelings of warmth and comfort of persons engaged in sedentary occupations or in very light work. But most of this is repetition of what is well known and has appeared in print many times before. The principal significance of the paper to those who are concerned with the heating and air conditioning of buildings lies in the conclusions which are drawn about the design or use of the plant. Yet even for the occupations or activities considered, there are still problems remaining to be solved. The electrical state of the atmosphere plays some role not fully understood, though recent investigations in America have shown changes in the ion content during smog, and have indicated some connexion between ion content and human well-feeling. The influence of clothing, too, extends beyond its purely insulating value. Changes in atmospheric humidity affect different fabrics in different ways, and LÖFSTEDT and RONGE have demonstrated how this phenomenon influences the bodily sensations. MISSENARD too has reflected on this point, and has shown that a person's sensations of the warmth of an environment depend very much on whether it is an immediate impression or one gained after a sojourn of a few hours' duration.

Dr. A. R. LIND (*The effect of heat on the industrial worker,* pp. 190–205) takes us away from the normal environment to that which is likely to cause heat stress. Again, it is largely a review paper, although the original material discussed is probably much less well known than Bedford's. This being so, it is perhaps a pity that after demolishing the effective temperature scale as a criterion of the physiological effects following exposure to conditions of high heat stress, he introduces the predicted 4–hour sweat rate without any indication of its meaning or its determination. Although Lind's own work, and that of the R.N. Personnel Research Committee, have been carried out with somewhat extreme conditions in view, Lind suggests that the predicted 4–hour sweat rate scale can be used to handle local heat problems which arise in certain industries. Nevertheless, it is apparent that a good deal of work remains to be done in connexion with appropriate environments for medium to heavy work under "normal" rather than abnormal conditions of temperature and humidity.

Two papers on cabin conditioning for military aircraft are of less general interest. Fl. Lt. J. BILLINGHAM (*Cabin air-conditioning in military aircraft. I. Physiological aspects,* pp. 208–214) poses a number of questions which are as pertinent to civilians in ordinary life as to RAF pilots; but no answers are attempted. In part II of this paper (*Engineering aspects,* pp. 215–221), D. J. DAY describes a fairly typical air cycle refrigerating plant, although there is a growing trend towards the use of conventional refrigerants.

B. G. LAWRENCE (*An outline of air-conditioning,* pp. 178–188) brings the reader back to earth with a brief summary of the principles underlying normal air-conditioning plant. Unfortunately, it is not a substitute for a text book: nor does it explain the factors which determine the type of plant chosen, (*e.g.,* for dehumidification), the system (high or low velocity) selected, or even whether air-conditioning or simple heating and ventilation is to be used. The air cleaner is an important component of the plant, and it is a pity that Lawrence dismisses this aspect in a single paragraph.

N. S. Billington

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

ECKARDT, R. E. **Experimental Carcinogenesis and the Problem of Food Additives.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1488–92.

One of the provisions in the United States Food and Drug Law Amendments (Public Law 85–929) states that "no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal." The author discusses the difficulties of interpreting and enforcing this provision. Techniques for producing tumours and cancers in animals rarely throw much light on the carcinogenic effect in man of a food additive or other substance. The reaction of different species to carcinogens differs widely,

depending on metabolic pathways and numerous other factors. A substance which readily produces tumours in mice may have no effect on rats and rabbits. In the field of food additives, experimental carcinogenesis is in its infancy.

The author concludes that "There are no magic formulas, no crystal balls, or simple manipulations of a slide rule that will permit the public health official to say whether a given compound will present a cancer hazard to the general public if it is permitted to enter the food supply". Decisions on this question can be reached only after the weighing of all the available facts and evidence, including the nature of the compound and its known biological effects, its probable concentration in the food supply and the function in food technology which it fulfils. More fundamental research is needed in this field. Because so much emotion is associated with the word "cancer," there is a tendency towards over-hasty decisions on carcinogenicity. *W. R. Aykroyd*

SIEGMUND, I. Untersuchungen über die Lebensdauer von Salmonellen und Shigellen in verschiedenartigen Lebensmitteln. [**Survival of Salmonella and Shigella Organisms in various Foods**] *Arch. f. Hyg. u. Bakt.* 1960, Oct., v. 144, No. 7, 550–63, 2 figs. [10 refs.]

This is an account of an extensive investigation of the periods of survival of 4 salmonellae—*Salm. typhi-murium, Salm.* newport, *Salm. enteritidis, Salm.* newington and of 2 shigellae—*Sh. flexneri, Sh. sonnei* in a large number of different foods and drinks at the temperatures of both 22°C. and 4°C.

The results of the investigation are fully described and set out in tables. The main conclusion was that all these organisms survive in many of the foods, but not in all, for an extremely long time. Butter and meat salad were foods in which the bacteria survived for the longest time; for example *Salm. typhi-murium* survived for 77 days in meat salad and 63 days in butter. A point of importance was that on average the organisms survived longer at 4°C. than at 22°C. Survival times in the other foods showed considerable variations and were not influenced significantly by ordinary acidity or salt content. A striking observation was that both groups of organisms survived for a very short time—usually less than 30 minutes—in red or white wine and only 10 minutes in curaçao. *M. E. Delafield*

UNITED KINGDOM. **Milk Composition in the United Kingdom. Report of an Interdepartmental Committee** [COOK, J. W., Chairman]. Cmnd. 1147. pp. iii + 92, 1 fig. [Refs. in footnotes.] 1960. London: H.M. Stationery Office. [5s.]

The committee was appointed "to consider the composition of milk sold off farms in the United Kingdom from the standpoint both of human nutrition and of animal husbandry and to recommend any legislative or other changes that may be desirable."

In addition to the main report, its summary and recommendations, there are 3 additional panel reports, those of the medical panel, the animal husbandry panel and the panel which considered the Hortvet (freezing point) Test for added water in milk. The panel reports were all accepted by the full committee and their conclusions were included in the main report.

The committee have interpreted the phrase "milk composition", in their terms of reference, as meaning those chemicals occurring naturally in milk; the bacteriology of milk and the possible presence of antibiotics, radioactive materials and hormones have therefore been omitted from consideration, other authorities being concerned with these aspects.

Milk is of importance in the human diet and nutritionally the most valuable fraction is the solids other than fat (s.n.f.) providing especially protein and calcium. Variations in the fat content are of much less importance, since the fat-soluble vitamins are normally adequately provided elsewhere in the diet. There is no conclusive evidence for a link between atheroma or coronary disease and the consumption of milk fat and thus no need to consider reducing the fat content of milk.

A slight decline in both the fat and s.n.f. fractions in England and Wales but not in Scotland has been observed over the last 30 years, the main objective of the dairying industry should be to arrest this decline and improve the s.n.f. content. Both statutory and marketing means to this end are advocated. There should be fixed minimum standards of 8·5% for s.n.f. and 3% for fat, the former to be adopted within 10 years and the latter within 5 years; these should apply only at the point of sale, certain special grades could be exempted. Milk should not be sold as a standardized product (*i.e.* adjusted to constant composition for s.n.f. and fat) and except for heat treatment milk should be sold as it comes from the cow. Producers should be encouraged to improve the s.n.f. content of milk by a differential payment scheme which should be introduced as soon as possible. In order that selective breeding could also be used to this end, progeny testing of AI [artificial insemination] dairy bulls should include performance records for s.n.f. and facilities should be made available for producers to have individual milk samples tested for s.n.f.

The report of the medical panel discusses in more detail the importance of milk in the diet and the reasons for advocating an increase in the s.n.f. fraction of milk and the possible, but not accepted, correlation between milk fat consumption and atheroma or thrombosis. The losses of riboflavine and ascorbic acid from milk by exposure to sunlight are considered; these, however, are not regarded as serious.

The animal husbandry report (31 pages) is almost as long as the main report and discusses in great detail trends in milk composition, the possible reasons for these changes and the factors involved in any improvements.

The Hortvet Test panel consider that the freezing point test for added water in milk is of sufficient accuracy to be accepted in legal proceedings, subject to certain provisos which are fully discussed, as proof of the presence or absence of added water and this recommendation is included in the report of the main committee.

The committee as a whole, feeling that the present

definition is inadequate, suggest a new legal definition of milk as follows:

"'Cows' milk' means the secretion, excluding colostrum, which can be gained by normal milking methods from the lactating mammary gland of the healthy, normally fed cow."

Three appendices are included, these are (a) a list of witnesses, (b) the present sale of milk regulations and (c) details of existing schemes to improve milk composition. There is a complete index. *P. L. Pellett*

See also p. 245, SCHILLINGER. [**Hygienic Evaluation of Agricultural Production with the Use of Herbicides.**]

FOOD POISONING

OTTE, H. J. & RITZERFELD, W. Massenerkrankung an Angina durch Streptokokken in Lebensmitteln. [**An Epidemic of Streptococcal Tonsillitis caused by Eating of Contaminated Food**] *Deut. med. Woch.* 1960, Sept. 9, v. 85, No. 37, 1625–8, 1662, 2 figs.

About half the 1,055 staff of a bank suffered from acute febrile sore throat within a period of 3 days; subsequent bacteriological examination of the healthy staff revealed a carrier rate of over 50% of group A type 9 haemolytic streptococci. The ill and infected persons had all eaten dinner prepared by the bank canteen on the day before the first patients sickened. The dish most probably responsible was a rice pudding prepared on one day and allowed to stand at room temperature for several hours between its preparation and consumption. *R. E. O. Williams*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

DONALD, G. F. **Tinea contracted from Kangaroos.** *Med. J. Australia.* 1960, May 28, v. 1, No. 22, 852–3.

A number of human cases of *Trichophyton mentagrophytes* infection, alleged to have been contracted from kangaroos, are reported in this article. In all cases outbreaks followed the introduction of a kangaroo into the home of the patients concerned, who kept them as pets.

The presence of fungus was usually established microscopically in the lesions and *T. mentagrophytes* was subsequently cultured from scrapings taken from them. The lesions were considered by the author to be typical of infection by this dermatophyte.

The possibility that kangaroos constitute a reservoir of *T. mentagrophytes* is most interesting. It is therefore unfortunate that the evidence available for this in the cases reported by the author is only circumstantial. However, although no investigations were carried out on the kangaroos concerned in these cases he is satisfied that it is reasonable to assume that these animals were the source of infection for the human patients. *C. J. La Touche*

MARPLES, Mary J. & SMITH, J. M. B. **The Hedgehog as a Source of Human Ringworm.** [Correspondence.] *Nature.* 1960, Dec. 3, v. 188, 867–8.

The authors isolated *Trichophyton mentagrophytes* from 7 of 26 hedgehogs collected in part of New Zealand. Hedgehogs "appear to constitute a hitherto unrecognized source of human infections".

UMNOVA, I. I. & FOMENKO, V. P. [**Trichophytosis of Field Mice causing Infection in Humans**] *Vestnik Dermat. i Venerol.* Moscow. 1960 v. 34, No. 11, 36–8. [In Russian.]

The English summary appended to the paper is as follows:—

"In rye thrashing collective farmers there developed an outbreak of trichophytosis produced by *Trichophyton gypseum.* 57 persons contracted the disease. Field mice, from whom cultures of *Trichophyton gypseum* were isolated, were the cause of infection."

ZUSSMAN, R. A., LYON, I. & VICHER, E. E. **Melanoid Pigment Production in a Strain of *Trichophyton rubrum*.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 708–13, 2 figs. [18 refs.]

UECKERT, H. Morphologie und Taxonomie der Dermatophyten. II.: Die Einordnung der Dermatophyten in das künstliche System der Fungi imperfecti. **[Morphology and Taxonomy of Dermatophytes. II. Classification of Dermatophytes in the System of Fungi Imperfecti]** *Bull. Pharmaceut. Res. Inst.* Osaka-Takatsuki. 1960, May, No. 26, 1–10, 6 figs. [29 refs.]

TOMOMATSU, S. **A Study on Griseofulvin. I. Comparison of Electron Microscopical Observation of Effect of Griseofulvin with that of Fungicidal Drug.** *Bull. Pharmaceut. Res. Inst.* Osaka-Takatsuki. 1960, May, No. 26, 11–20, 17 figs. [18 refs.]

REISS, F., KORNBLEE, L. & GORDON, B., with the technical assistance of J. VILLAFANE. **Griseofulvin (Fulvicin) in Treatment of Fungous Infections of the Hair, Skin and Nails with special reference to Mycologic Changes produced during Therapy.** *J. Investigative Dermat.* 1960, Apr., v. 34, No. 4, 263–9, 4 figs. [11 refs.]

After surveying previous literature on griseofulvin therapy, the authors record their experience with this drug.

The patients who were treated by them included: 25 children presenting with tinea capitis due to *Microsporum audouini*, 1 child with tinea capitis due to *M. canis* and 5 children with tinea capitis due to *Trichophyton tonsurans*; also included were: 3 patients with tinea glabrosa due to *T. rubrum*, 4 with tinea pedis due to *T. mentagrophytes*, and lastly, 5 with onychomycosis due to *T. rubrum*, and 1 due to *T. mentagrophytes*.

The dosage administered to the children presenting with tinea capitis was 250 mgm. twice daily while the adults suffering from tinea pedis and onychomycosis received 500 mgm. twice daily. No local therapy was administered.

Results were, on the whole, in agreement with those of previous investigators using this drug clinically; thus, for example, clinical effects manifested themselves within the first week in the case of tinea capitis due to *M. audouini*, and cure was achieved in these cases in a mean of 44 days, while *T. tonsurans* infections were cured in a mean of 53 days.

Some morphological features of the fungal parasites on the hair shaft which were observed by the authors were interpreted by them as reflecting some profound metabolic disturbance due to the action of this drug during the course of treatment.

During cultural investigations it was observed that scrapings from the scalp were often productive of positive cultures when faintly fluorescent hairs were culturally negative. *C. J. La Touche*

SCHWARZ, J. & LOUTZENHISER, J. K. **Laboratory Experiences with Griseofulvin.** *J. Investigative Dermat.* 1960, May, v. 34, No. 5, 295–9, 6 figs. & 1 graph.

The authors of this article investigated the *in vitro* sensitivity of various pathogenic and non-pathogenic fungi and actinomycetes to concentrations of griseofulvin ranging from 80 μgm./ml. to 0·15 μgm./ml. and the effect of griseofulvin plus penicillinase on a number of dermatophyte species. They also administered this drug to mice in order to ascertain its effect on their development.

The results of the *in vitro* tests showed that the inhibitory effect of griseofulvin was confined to the dermatophytes which were tested, and that this effect could be well demonstrated in their morphology when griseofulvin was placed on the agar in the petri dish at a distance from the advancing fringe of already established colonies.

This morphological alteration showed itself within a few hours as undulations in the main hyphae and curling of the main branches. Ultimately the mycelium became degenerate and clumped.

The result of administering the drug to young mice was that small amounts produced a considerable increase in weight after 10 days, whereas "large amounts had definite inhibitory effect on the development". Administration of the drug in a dosage under 1 gm. per kgm. per day "had no recognizable effect on spermatogenesis" but dosage above 1·3 gm. per kgm. per day given for 18 to 24 days resulted in "considerable decrease, or complete suppression of spermatogenesis". *C. J. La Touche*

DOSTROVSKY, A., RAUBITSCHEK, F., EVEN-PAZ, Z. & AXELRAD, B. **The Treatment of Tinea Capitis with Oral Potassium Iodide. A Preliminary Report.** *J. Investigative Dermat.* 1960, May, v. 34, No. 5, 347–9.

A previous report (TULTCHINSKY-GOLDSTEIN, *Harefuah*, 1958, v. 55, 291) prompted the authors of this article to explore further the therapeutic potentialities of orally administered potassium iodide in infections due to dermatophytes.

77 patients, including children of each sex, 35 males and 42 females, whose ages were between 1 year and 14 years, as well as 1 female aged 22 years and 4 mothers, were selected for these trials. Most of them had recently returned to Israel from other Mediterranean countries.

The dermatophytes isolated from these patients were: *Trichophyton violaceum* in 47 cases and *T. schönleini* in 9 cases. Mycological investigations were not carried out in 17 cases and 4 cultures were sterile.

Potassium iodide was administered in the daily dosage of 1·0 gm. to children aged up to 3 years, 2·0 gm. to children of 3–7 years old, 2·5 gm. to children from 7–12 years old, and 3 gm. to older children and adults.

The results achieved included the cure of 40 patients out of 68 with tinea capitis due to *T. violaceum* within periods which varied from 30 days or less to 130 days or more, while 2 out of 9 cases of favus were cured in less than 30 days. *C. J. La Touche*

ZIPRKOWSKI, L., SCHEWACH-MILLET, M. & KRAKOWSKI, A. **[Treatment of Tinea Capitis with Oral Potassium Iodide. Review of 29 Cases]** *Harefuah.* Jerusalem. 1960, Nov. 1, v. 59, No. 9 [in Hebrew 265–6. English summary 266].

The English summary appended to the paper is as follows:—

"29 patients suffering from tinea capitis (28 due to *T. violaceum* and one due to *M. audouini*) were treated with potassium iodide by mouth. Clearing of lesions was achieved in 12 patients, although 2 of them again showed signs of infection during the follow-up period. Treatment did not succeed in the other 17 patients either because of inefficacy of the drug or because of premature cessation of the medication. 14 patients suffered from various symptoms during the treatment. Half of these were clearly side effects of the drug.

"The results were far inferior to those obtained with griseofulvin. Potassium iodide is clearly not suitable for the eradication of the disease."

AL-DOORY, Y. **Free Lipids and Phospholipid Phosphorus of *Histoplasma capsulatum* and other Pathogenic Fungi.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 565–6.

"The yeast phase of *Histoplasma capsulatum* contains larger amounts of free lipids and phospholipid phosphorus than the mycelium of the same fungus and that of *Hormodendrum pedrosoi* and *Microsporum canis.* Also the still cultures of *H. capsulatum* and *H. pedrosoi,* which contain mycelium and spores, have a greater amount of free lipids and phospholipid phosphorus than their shake cultures, which contain mostly mycelium."

BOX, Edith D. & MCSHAN, Oleta B. **Chemotherapy of Experimental Histoplasmosis.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 3, 379–94. [20 refs.]

These authors have tested the action of large numbers of drugs on *Histoplasma capsulatum in vitro* and *in vivo.* Those tested *in vitro* include various antibiotics, acridines, quinolines and a very miscellaneous additional group: *in vivo* tests were done with many of these, with further antibiotics, various anti-metabolites, parabens and sulphadiazine. [The reasons for considering some of these drugs worth testing seem rather far-fetched: antimalarials were included because, as in histoplasmosis, a drug affecting this disease must be capable of acting intra-cellularly—this regardless of the fact that the causes of the 2 diseases belong to different kingdoms.]

Naturally most had no effect on the acute infection in mice produced by large intravenous inoculum of a suspension of the yeast phase: some accelerated death. Ethyl vanillate, which has been recommended for treating the human disease, had no effect in the mouse. Sulphadiazine was regularly protective against lethal infection, but did not sterilize the affected organs. Among antibiotics, amphotericin B (given intravenously) was the most effective: the degree of effect varied with the number of doses, and with the form used, the more soluble desoxycholate acting best. Mice so treated not only survived, but yielded no growth from eventual cultures of spleen and liver. Eulicin had a similar though less constant effect, but failed against infection with a different strain. Nystatin had a slight effect when given subcutaneously as a suspension: when dissolved in propylene glycol and administered intravenously it merely accelerated death. Human gamma globulin did not enable an inadequate dose of amphotericin B to save life [the dose of the former was 10 ml. intraperitoneally to a 20 gm. mouse: there is no actual evidence that the injection of this enormous volume of fluid did not contribute to the animals' death], but previous incubation of the inoculum in gamma globulin rendered it non-lethal. *L. P. Garrod*

WATT, D. L. & LINTON, W. T. R. **Sporotrichosis treated by Griseofulvin—a Failure.** *Canadian Med. Ass. J.* 1960, Nov. 19, v. 83, No. 21, 1103.

"A patient with sporotrichosis has been carefully followed up. Over the first three months of his illness there was no spontaneous improvement. While the patient received griseofulvin therapy, the disease progressed.

"Potassium iodide therapy resulted in remarkable improvement within three weeks and apparent cure after three months, when therapy was stopped. One subcutaneous lesion recurred two months later and responded well to further iodide therapy."

LAMEDICA, G. M. & PERETTI, M. Rapporti tra caratteri morfologici e potere patogeno *Candida albicans.* **[Relation between the Morphological Characters and the Pathogenicity of *Candida albicans*]** *Giorn. di Malattie Infettive e Parassit.* 1960, Aug., v. 12, No. 8, 390–93, 3 figs. [25 refs.]

RAO, G. R., RAMAKRISHNAN, T. & SIRSI, M. **Enzymes in *Candida albicans.* I. Pathways of Glucose Dissimilation.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 654–8, 6 figs. [18 refs.]

SACCOMANI, F. La nistatina e l'anfotericina B per trattamento locale in 91 lattanti affetti da dermatosi varie di cui 39 da *Candida albicans.* **[Local Treatment with Nystatin and Amphotericin B in 91 Infants with Dermatoses of which 39 were due to *Candida albicans*]** *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 262–7. [44 refs.]

The following is a translation of the author's summary:—

91 infants suffering from three types of skin conditions (gluteal intertrigo, diffuse eczema, Leiner's disease), 39 of which were due to *Candida albicans,* were treated by local application of antimycotic preparations. 72 were

treated with Nystatin ointment and 19 with Amphotericin B ointment. With Nystatin optimum results were obtained in peri-anogenital intertrigo and moderate results in diffuse eczema and Leiner's disease. Amphotericin B was inferior to Nystatin in therapeutic action.

H. J. O'D. Burke-Gaffney

HENIS, Y. & GROSSOWICZ, N. **Studies on the Mode of Action of Antifungal Heptaene Antibiotics.** *J. General Microbiol.* 1960, Oct., v. 23, No. 2, 345–55, 8 figs. [27 refs.]

This paper is part of a doctoral thesis submitted by the first-named author in the Hebrew University, Jerusalem. It is concerned chiefly with the action on *Candida albicans* and other yeast-like fungi of heptamycin, a heptaene antibiotic (as are ascosin, candicidin and trichomycin) first described by the authors 3 years ago. The main findings in numerous experiments on the action of this substance on the metabolism of yeast-like fungi were that it reduced the oxidation of pyruvate, lactate and trehalose, but not that of glucose and acetate, and secondly that it inhibited phosphate uptake. The authors believe the latter effect to be mainly responsible for its fungistatic action. *L. P. Garrod*

ALLGÉN, L. G. & FRISK, Å. **A Study of a New Antifungal Substance, Tetrahydrofluorenone.** *Acta Med. Scandinavica.* 1960, Mar. 10, v. 166, No. 3, 161–74, 5 figs.

The substance which is the subject of this report is 1,2,3,4-tetrahydro-9-fluorenone (THF). It is insoluble in water but soluble in organic solvents such as alcohols, cyclohexane and vegetable oils. It is sensitive to oxidation and to light. It may be heated for a short time for sterilization purposes without decomposing.

The authors carried out a number of *in vitro* tests in order to evaluate its antifungal effect. The test organisms included several species of *Candida* and one of *Torulopsis* (*Cryptococcus*). Against these organisms the antifungal effect was mainly fungistatic.

Clinical trials were also carried out. The 40 patients concerned included some suffering from mycotic stomatitis, broncho-pulmonary disease or empyema of the pleura, and a group of diabetic patients in whom diabetes was complicated by cystitis.

THF was administered to them orally, as well as by instillation into the bladder in the case of those suffering from cystitis.

Favourable response to treatment with this drug is claimed by the authors for 23 of their cases, although some of the patients who were very seriously ill actually died during treatment.

Side-effects to the administration of THF included only slight gastro-intestinal disturbances which did not necessitate interruption in the treatment.

Tests to ascertain whether the drug was absorbed showed that when it was administered orally it could be recovered subsequently in the urine but not in the serum.

C. J. La Touche

HAUSER, T. E. **Cryptococcosis: A Case Report.** *Ann. Intern. Med.* 1960, Oct., v. 53, No. 4, 816–22, 3 figs.

"A 56 year old man developed a severe, acute cryptococcic meningo-encephalitis and, despite amphotericin B therapy, died 27 days after the onset of his illness. In addition to the severe meningo-encephalitis, autopsy revealed cryptococcus granulomas in the upper lobes of both lungs."

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

BOLLIGER, W. **On the Incidence of Tuberculosis in Victoria.** *Med. J. Australia.* 1960, Oct. 1, v. 2, No. 14, 528–32.

During the period 1954–59 413,245 immigrants entered Australia of whom 43·5% settled in Victoria. The largest numbers were British, Italian, Dutch, German and Greek in that order. Before leaving their own countries all had been medically examined to exclude disease. The examination had included X-ray of the chest.

There is a high level of employment in Victoria and migrants are assured of work and maintenance of their families at a reasonable standard.

The number of deaths from tuberculosis has declined steadily but the number of new cases of tuberculosis has not declined appreciably; it was 813 in 1957, 776 in 1958

and 862 in 1959. Women account for about one-third of the cases, and a higher proportion of women than of men are in the younger age-groups.

The trend of tuberculosis is also illustrated by tuberculin surveys. Reactor rates in 14-year-old children in the metropolitan area were 7·56% in 1954 and 6·32% in 1958; the rates in the rest of the state were 5·86% and 5·9% respectively. The rates are higher in immigrant than in native children.

Analysis of cases by the stage of the disease at diagnosis showed that a higher proportion of women than of men had minimal disease. This may be due to the women being younger, better educated in health matters, under closer medical supervision or because they live harder lives than men on a 40-hour week and succumb earlier to the illness.

The presence of a large proportion of reactors in the population (especially among immigrants) suggests that the morbidity rate from tuberculosis will not fall below a certain minimum and may even increase. The present policy of BCG vaccination of all non-reactors at 11 years of age and of contacts and others specially exposed to risk should continue.

The author wonders if Victoria in its favourable situation should not open its doors to immigrants [even with tuberculosis] who would otherwise be homeless and stateless for the rest of their lives. "This question is particularly pertinent in Victoria, where there are empty beds in sanatoria and good facilities for successful treatment."

Mass radiography surveys discover about one-fifth of the notified cases. The present level of tuberculosis would not justify compulsory periodical X-ray examination of the whole population. Bollinger suggests instead compulsory examination on applying for old-age pension, prior to marriage and as part of insurance examination. Teachers and others in close contact with children should also be periodically subjected to X-ray examination.

H. G. Calwell

COMSTOCK, G. W. **A Comparison of Purified Tuberculins in the South-Eastern U.S.A.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 683–8, 1 fig. [10 refs.]

Simultaneous Mantoux tests with 5 TU of PPD-S and RT 19–20–21 were given to 1,617 schoolchildren in Georgia and Alabama, U.S.A. Previous reports on these tuberculins had shown that they were nearly equivalent when used in doses of 5 TU [this *Bulletin,* 1959, v. 34, 429].

640 children (40%) in the present group gave reactions of the same size, 709 (44%) gave larger reactions to RT than to PPD-S and 268 (17%) gave smaller reactions to RT than to PPD-S.

By the criterion of 6 mm. or more of induration as positive 1,169 of the children were non-reactors and 245 reactors to both antigens. However 171 reacted to RT but did not react to PPD-S whereas only 32 were negative to RT and positive to PPD-S.

Analysis by diameter of induration showed that nearly 75% had less than 4 mm. to PPD-S and 55% less than 4 mm. to RT. Only 18% had reactions of 4–11 mm. to PPD-S compared with 39% to RT. Both antigens evoked fairly similar proportions of reactions of 12 mm. or more —8% with PPD-S and 6% with RT.

The antigen most likely to give the larger reaction varied with the subject's level of sensitivity to tuberculin. Those with low levels gave larger reactions to RT than to PPD-S and those with high levels reacted more strongly to PPD-S than to RT. The same pattern was seen in each group tested *viz.* whites, Negroes, BCG-vaccinated and unvaccinated persons.

As most low-grade tuberculin sensitivity in the area is attributable to infecting agents other than *Myco. tuberculosis* [*ibid.,* 1960, v. 35, 455] it is seen that RT detects sensitivity to at least some of these agents better than PPD-S. "Until much more is known about the nature of tuberculin sensitivity in different population groups, it will be unwise to assume that two tuberculin tests which yield similar responses in one population will do so in other population groups." *H. G. Calwell*

ROSENTHAL, S. R. & LIBBY, J. E. P. **Simultaneous Multiple Tuberculin Testing.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 689–92, 1 fig. [15 refs.]

Infants aged 2–5 days were vaccinated with BCG and 3–5 months later tested with 10 and/or 100 TU of OT given intracutaneously, separate arms being used for each dose. In all 306 infants were tested with 1 dose and 305 with both doses.

The mean diameter of induration to 10 TU in the single-test group was 17·6 mm. and in the double-test group 13·4 mm. The mean of the 305 reactions to 100 TU was 21·5 mm. which was 61% greater than the mean of the 305 reactions to 10 TU of the same infants. Thus single instead of double testing increased the size of the reaction more than half as much as did increasing the dose of tuberculin 10-fold.

With the single test (10 TU) there were fewer reactions in the 3 lower levels of distribution by size and more in the upper 2 levels than when the double test was used (10 TU along with 100 TU).

The authors have been unable to find any previous report on the effect of simultaneous multiple testing on the size of the tuberculin reaction in man. A parallel phenomenon has however been seen in guineapigs [this *Bulletin,* 1954, v. 29, 927].

"The present interaction suggests competitive drawing upon an antibody production which is not unlimited in the period of the reaction." *H. G. Calwell*

BJERKEDAL, T. **Comparative Sensitivity of School-Children in Oslo to Two Mycobacterial Antigens PPD-S and PPD-B.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 3, 209–16, 3 figs.

Sensitivity to antigens made from atypical mycobacteria has not been greatly studied in Europe. A comparative sensitivity study was therefore undertaken in Oslo with PPD-S and PPD-B (prepared from the Battey bacillus [this *Bulletin,* 1959, v. 34, 816]).

Tuberculin testing is done routinely on Oslo school-children, and there is a register with details of the sensitivity and BCG vaccination of each child. It was thus

possible to exclude vaccinated children from the study and to obtain groups of "natural" reactors and non-reactors.

In the 3 schools participating in the enquiry there were only 47 children classified as natural positives of whom 43 took part, and to these were added 3 who had shown small reactions and 2 originally classified as reactors and later as non-reactors. The group of "natural" reactors consisted therefore of 48 children of whom 5 had doubtful positive reactions.

Each of the 48 was now tested with 2 antigens together with 2 negative children selected randomly. The groups did not represent a random sample of the total elementary school population.

The Mantoux test was used with 0·0001 mgm. of PPD-S and PPD-B given at the same time in each forearm. All the tests were given by the same nurse who also read all the reactions after 48 hours. Reactions on the right arm were read first with the child holding the left arm behind the back.

In the group of 48 original reactors the PPD-S reactions centred round 21 mm. of induration and PPD-B around 15 mm. Correlation between reaction sizes was only slight; except in 1 child the reaction to PPD-S was larger than that to PPD-B. 6 of the children reacted to PPD-S with less than 5 mm. of induration including 4 with doubtful reactions to the earlier routine tests. 4 of the 6 with a reaction to PPD-S of less than 5 mm. had a reaction to PPD-B of 5 or more mm.

In the group of 297 original non-reactors 296 had a reaction to PPD-S of less than 5 mm., and 32 had a reaction to PPD-B of 5 or more mm. Indurations to PPD-B were less sharply delimited than to PPD-S. This was also true for erythema.

The results support the view that sensitizing agents other than the ordinary human type tubercle bacillus are acting in Oslo and that those other agents, though probably not the Battey bacillus, are antigenically more closely related to it than to the human type tubercle bacillus. Further investigation is called for.

H. G. Calwell

HORWITZ, O. & KNUDSEN, J. **Comparison between Attenders and Non-Attenders at the Danish Mass Tuberculosis Campaign, 1950–52. Tuberculosis Morbidity and General Mortality in the Two Groups during the First Four Years of Follow-up.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 669–80, 5 figs. [11 refs.]

It is important to know whether the incidence of pulmonary tuberculosis discovered in a mass radiography survey is representative of the incidence in the whole general population or whether in fact it is higher in those who have failed to attend for examination.

In order to answer the question for Denmark the authors have compared the incidence of the disease and the general mortality in those who co-operated in the mass tuberculosis campaign of 1950–52 and in those who did not take part.

The campaign, which included mass radiography and BCG vaccination, took in persons aged 15–34 years. It was carried out in the provinces where three-quarters of the total population of Denmark live. Excluding those known to have or to have had tuberculosis there were 390,641 males and 387,433 females. Attenders numbered 508,783 and non-attenders 269,291.

There were some differences in the composition of the 2 groups. For example 53% of the attenders and 45% of the non-attenders were females among whom, in the age-group concerned, tuberculosis morbidity is higher than in males; this would tend to exaggerate the morbidity rate. Another difference was that there were relatively more rural dwellers among the attenders than the non-attenders, and this would tend to reduce the tuberculosis morbidity rate, which is higher in towns than in the country.

There was also some difference in the age composition of the 2 groups but this was compensated for by using age-standardized rates calculated on the basis of the rates in 5-year age-groups throughout.

The extent of BCG vaccination before the campaign was 22% in both groups but the returns were not entirely complete, and it was considered that the true extent of vaccination was higher than this.

The incidence of respiratory tuberculosis in males in the 4 years after the campaign was 26 per 100,000 in attenders and 40 in non-attenders. The rates in females were 31 and 59 respectively. The total morbidity rate among male attenders was 38 and among male non-attenders in the same period 40. The rates for females were 49 and 59 respectively.

There was therefore a higher incidence of tuberculosis in non-attenders than attenders. Part of the difference was explicable by the difference in place of residence mentioned earlier. Another reason might be the larger number of attenders vaccinated with BCG in the campaign as a result of which the total percentage of vaccinated non-attenders was only about one-half that of attenders.

During the follow-up period the general age-standardized mortality rates in male attenders and non-attenders were 90 and 127 per 100,000 respectively. Among the females the rates were 54 and 91 respectively. The higher mortality among the non-attenders is presumably due to the fact that a number of non-attenders did not attend because of illness. The higher mortality was not connected with a special group of diseases.

The type of pulmonary tuberculosis discovered among the attenders and non-attenders was of equal severity, and it was not the authors' experience that many of the cases discovered in the survey were clinically or epidemiologically unimportant. *H. G. Calwell*

ERIN, L. **Detection of Pulmonary Tuberculosis by Sputum Survey.** *Tubercle.* 1960, Oct., v. 41, No. 5, 363–6.

The author investigated the efficacy and cost of sputum examination on a large scale as a supplement to mass radiography. The work was done in a Welsh mining town of 26,128 inhabitants in which there were 18 notified cases of tuberculosis in 1958 and the tuberculin reactor rate in 13-year-old children was 12%.

A nurse visited 1,395 houses and invited adults with sputum to provide a specimen for examination. 910 householders agreed to co-operate. 2,001 of the 3,138

adults sent specimens, of which 1,982 were successfully cultured.

Tubercle bacilli were found in 4 specimens which came from men aged 37, 61, 63 and 73 respectively. All showed radiological evidence of tuberculosis; none had sought medical advice and all were mixing freely in the community. Cavitation was absent.

The response to the survey was compared with that to mass radiography; it was better in the older and worse in the younger age-group.

In 1958 the Welsh Mass Radiography Service had a discovery rate of active pulmonary tuberculosis of 1·8 per 1,000 examined. The yield of the present sputum survey was 2 per 1,000. Of course it failed to discover sputum-negative cases and other lesions.

The cost of the sputum survey was much less than that of a mass radiography survey but if it had been done on a large scale necessitating new laboratory facilities it would have been much more costly than mass radiography. A trial of sputum surveys among pensioners in homes for the aged would likely produce a high yield and reach more of the older people than a radiography survey. *H. G. Calwell*

Bell, W. J., Brown, P. P. & Horn, D. W. **Prednisolone in the Treatment of Acute Extensive Pulmonary Tuberculosis in West Africans.** *Tubercle.* 1960, Oct., v. 41, No. 5, 341–51. [18 refs.]

This is a very well controlled investigation to determine whether the addition of prednisolone to standard drug therapy in West Africans who have acute pulmonary tuberculosis is of any significant advantage. Standard drug therapy by the 3 drugs was given to all patients. In the prednisolone group after 1 week's drug treatment prednisolone was added and continued over a period of 8 weeks in a dose of 5 mgm. 4 times daily. During the 10th and 11th week the dose of prednisolone was gradually dropped, and none was administered during the last (12th) week in hospital. 45 patients were in the prednisolone-treated group, and 46 in the control group at the start of the investigation. At the end of the 3 months 41 patients remained in the prednisolone group, and 44 in the control group. The 2 groups seemed, from all points of view, closely comparable. Regular assessments were made at the end of the first, second, and third month, at the termination of which the investigation was closed. Well compiled tables are given of the results of the various investigations.

The conclusions arrived at were:—that at the end of the first month the general condition of the patients in the prednisolone group had improved more than in the control group, but this improvement gradually tailed off and at the end of 3 months there was very little difference. Apart from this there was no evidence that any statistically significant difference occurred in the patients in the prednisolone group compared with the control group, especially from the point of view of conversion of sputum and radiological improvement. (An interesting point noted was that the circulating white cells increased in numbers in the prednisolone group.) This was disappointing at it was hoped that the use of prednisolone would increase the rate of improvement in the patients so that at the end of 3 months, which was about the maximum time which could be allowed in hospital, the prednisolone group would have improved a good deal compared with the control group, but this was not so.

It is concluded that under the particular circumstances of the trial no advantage was obtained by the routine use of prednisolone. *F. H. Young*

Mathur, K. S., Prasad, R. & Mathur, J. S. **Intrapleural Hydrocortisone in Tuberculous Pleural Effusion.** *Tubercle.* 1960, Oct., v. 41, No. 5, 358–62. [10 refs.]

This paper reports a controlled trial on 50 patients with tuberculous pleural effusion admitted to the Sarojini Naidu Hospital, Agra, India. 25 patients were allocated at random to each group; all were treated with streptomycin daily, and isoniazid. In the hydrocortisone group 250 mgm. in the first 10 patients, and 125 mgm. in the remaining 15, were injected intrapleurally at one injection. In the hydrocortisone group the fever settled to normal in 24 hours of the administration of hydrocortisone in 21 out of 25 patients, and within 48 hours in 2 others. The remaining 2 cases were apyrexial at the start. In the control group the fever settled to normal gradually in 2–4 weeks, or longer, in the majority of cases, and not earlier than 1 week in any case. In the hydrocortisone group the absorption of fluid was striking in 18, good in 3, fair in 2, and unsatisfactory in 2. In the control group, no results were striking, 2 were good, 7 fair, and 16 unsatisfactory. Pleural biopsies in the hydrocortisone group were taken at the time of the injection and typical tuberculous granulation tissues found in 9, and non-specific pleurisy in the remaining 16. In the hydrocortisone group, 16 showed no residual pleural thickening and 7 were left with slight haze or pleural thickening in the costo-phrenic angles. In the control group variable grades of thickened pleura were left in most of the patients in whom the fluid was absorbed.

The authors conclude that instillation of hydrocortisone into pleural effusions represents a great advance in treatment. *F. H. Young*

Wynn-Williams, N. & Shaw, J. B. **Is Cavity Closure in Pulmonary Tuberculosis influenced by Bed-Rest?** *Tubercle.* 1960, Oct., v. 41, No. 5, 352–7.

It is now fairly well agreed that no great advantage is obtained in minimal tuberculous lesions of the lung by the use of bed rest, but in more advanced cases there is difference of opinion. This paper deals with a group in which there was cavitation; the patients were divided into groups determined by the apparent size of the cavity as shown by antero-posterior films and tomography. Between July 1957 and March 1959, 70 patients entered the trial in the chest units at the Bedford General Hospital, and St. Mary's Hospital, Luton. 62 patients completed the trial, 29 on the bed-rest group, and 33 on the exercise group. The two groups seem to have been very fairly comparable. The follow-up period extended from a minimum of 1 year to a maximum of 2½ years. In the rest group the patients were confined to bed until either cavity closure took place, or 6 months had elapsed,

when the patient was reassessed for further treatment if necessary. It is emphasized that the bed rest was simple bed rest, and not bed rest supplemented by postural therapy. The exercise patients were allowed to do what they liked unless they felt ill.

At the end of 6 months, no statistical difference was found between the 2 groups in the time taken for cavity closure, sputum conversion, and reduction of sedimentation rate. A further assessment after 12 months showed similar results between the 2 groups. The patients in the rest group were away from work twice as long as those in the exercise group. The drug treatment was similar in all respects, usually streptomycin, isoniazid and PAS being given for 3 months, followed by isoniazid and PAS for periods up to about 2 years. The exercise group had the advantage that there was less neurosis arising in patients about their ability to take up normal activities again. The advantage of hospital or sanatorium treatment does not lie in the value of bed rest, but in the ability to make certain that the patients take their drugs regularly. *F. H. Young*

JESIOTR, M. **[A Case of Severe Hypersensitivity to PAS simulating Infectious Mononucleosis]** *Harefuah.* Jerusalem. 1960, Nov. 1, v. 59, No. 9 [in Hebrew 267–8, 1 fig. on pl. (13 refs.) English summary 268].

The English summary appended to the paper is as follows:—

"A clinical picture due to hypersensitivity to P. A. S. is described, and the medical literature is reviewed. In addition to fever, scarlatiniform rash, lymphadenopathy, and liver enlargement, a blood picture simulating early infectious mononucleosis was noted. It is important not to mistake the picture for infectious mononucleosis, because continued administration of P. A. S. may be fatal".

REISS, J. & TOWNSEND, S. M. **Cycloserine: Growth Enhancement Phenomenon found during Sensitivity Studies: Clinical Implications.** *J. Lab. & Clin. Med.* 1960, Oct., v. 56, No. 4, 607–12, 2 figs. [11 refs.]

The report describes a series of susceptibility studies made to test, *in vitro,* the bacteriostatic action of cycloserine compared with isoniazid, streptomycin, and PAS antibiotics, on virulent strains of *Myco. tuberculosis.* Resistance to cycloserine occurs early in patients treated with the three antituberculous drugs. In 45 of the 62 patients, with 85 cultures, there was initial resistance to cycloserine, whereas 17 patients with 35 cultures were susceptible to a minimum of 20 μgm. per ml. and resistant to the 2 lower concentrations. All of the 17 initially sensitive to cycloserine were also sensitive to at least 1 of the other 3 antibiotics. It was also found that those 17 patients who showed initial sensitivity to cycloserine were sensitive to a minimum concentration of 20 μgm. per ml. In the tubes that contained lower concentrations of the drugs growth was either equal to or more abundant than that in the control tubes, especially in the case of organisms obtained from 45 of the patients who were initially resistant to cycloserine.

It appears, therefore, that *in vitro,* in concentrations where the organisms were partially resistant to cycloserine, the addition of small concentrations of cycloserine actually enhanced the growth of the organisms.

F. H. Young

LAUCKNER, J. R. **Acceptability of Ethionamide (1314TH) in Nigerian Patients.** *Tubercle.* 1960, Oct., v. 41, No. 5, 367–9.

Ethionamide is an effective tuberculostatic drug of low toxicity but it is badly tolerated at optimum dosage (15–20 mgm. per kgm. daily) because of gastro-intestinal upset. It is the author's impression that Nigerian patients tolerate PAS better than Europeans, and he therefore carried out a trial of the acceptability of ethionamide.

21 patients with pulmonary tuberculosis were admitted to the study and treated with ethionamide alone as outpatients for 12 weeks. They were then kept under observation for 1–3 months. The following were the criteria of selection: organisms thought to be resistant to at least 2 of the standard drugs; patient not eligible for surgical treatment; general condition satisfactory; no past or present isoniazid neuropathy; patient able and willing to attend weekly.

The drug was given in dosage of approximately 15–17 mgm. per kgm. daily; tablets of 125 mgm. were used and the daily dose was divided into 2 equal portions to be taken in the morning and evening after meals. Initially enteric-coated tablets were used but about half-way through uncoated tablets were used.

There was weekly supervision of the patients, and before starting, full examination was made. The chest was examined by X-ray immediately before the start and at the end of 12 weeks' treatment. Chloroquine was given to prevent malaria which might have caused a fall in haemoglobin.

All patients completed the 12 weeks' treatment; 5 missed 1 week, 1 missed 3 weeks and 1 missed 4 weeks. 9 patients admitted to no gastro-intestinal symptoms, 3 had transient diarrhoea probably unconnected with the drug, 6 had transient anorexia, abdominal pain or vomiting once or twice only. 4 patients experienced more persistent epigastric pain or vomiting which was never severe and in 2 cases stopped completely without interrupting the treatment.

11 patients complained of excessive salivation, sore mouth or sore tongue. On the basis of clinical resemblance to deficiency of B vitamins yeast was given, and in 6 patients there was great improvement or clearing. In none of them was it necessary to interrupt the treatment.

There was a definite tendency to lose weight which was not connected with clinical deterioration. It tended to be continuous during treatment and did not follow the rise and fall in sputum positivity. It was probably due to impairment of appetite by the drug.

It was tentatively concluded that a routine dosage of 1 gm. daily could be used in Nigerian patients. Ethionamide is a potentially useful drug for the treatment of tuberculosis in the tropics and its use should be further explored. *H. G. Calwell*

DORMER, B. A. & WOOD, M. M. **Prophylactic Isoniazid in Nurses in a Tuberculosis Hospital.** *Lancet.* 1960, Oct. 15, 837–40, 5 figs.

This paper deals with the incidence of tuberculosis in some 1,900 non-European nurse aides in a tuberculosis hospital in Durban. 83·9% of the nurses were tuberculin positive on appointment. Between 1946 and 1949, 55 cases of tuberculosis arose among these nurse aides. The incidence of tuberculosis fell fairly dramatically after the introduction of BCG in 1950, but after the introduction in 1955 of prophylactic isoniazid, 300 mgm. daily in a single dose given to about 600 nurse aides, no cases appeared until 1958 when one was diagnosed, followed by 3 in 1959. The fact that nurses when on leave were not taking isoniazid may be a factor. 6 illustrative case records are given. *F. H. Young*

ACRED, P. & BROWN, D. M. **The Antitubercular Properties of a Series of Thiols and Sulphides.** *Brit. J. Pharmacol. & Chemotherapy.* 1960, Dec., v. 15, No. 4, 485–95. [16 refs.]

LORBER, J. & MENNEER, Peggy C. **Freeze-Dried B.C.G.** *Arch. Dis. in Childhood.* 1960, Oct., v. 35, No. 183, 492–4. [10 refs.]

Clinical trials of British freeze-dried BCG vaccine have been made by several workers since the introduction of the vaccine in 1955 [this *Bulletin,* 1956, v. 31, 1260; 1958, v. 33, 117, 572, 1037; 1959, v. 34, 623].

The purpose of the present paper is to report on the efficiency of the commercially available vaccine and to report on the follow-up of children who were re-examined 1 year after vaccination and had all been vaccinated with commercially available vaccine. The children, who were mostly contacts, numbered 1,103.

In addition 1,005 children who had been vaccinated with various trial batches of vaccine were recalled 1 year after vaccination. 434 had been given vaccines of widely differing viability counts ($0{\cdot}1 \times 10^6$ to 23×10^6 per ml.) and 571 had received more uniform vaccines ($2{\cdot}4 \times 10^6$ to $8{\cdot}0 \times 10^6$ per ml.).

The routine pre- and post-vaccinal test was the jelly test. If the result was doubtful or was negative after vaccination or had not been done the child was given the Heaf test. Those still negative were tested intracutaneously with 100 TU. The same procedure was used 1 year after vaccination.

All but 4 of the 1,103 children who had received commercial vaccine became reactors 6 to 8 weeks after vaccination, and only 10% of those who had the jelly test required a Heaf test to demonstrate conversion.

Of the 434 children vaccinated earlier with experimental batches 99·7% were reactors 1 year after vaccination, and the only 2 non-reactors were not tested further. 83 children who had received the weakest vaccine ($0{\cdot}14 \times 10^6$ ml.) and whose post-vaccinal conversion rate was only about 56% were all reactors 1 year after vaccination.

It is concluded that the British freeze-dried BCG vaccine now available is safe and convenient to use. It causes neither ulceration nor adenitis and gives almost 100% conversion rate. Sensitivity remained for at least 1 year after vaccination. *H. G. Calwell*

BANG, J., ENGBAEK, H. C. & NIELSEN, E. **Osteomyelitis following BCG Vaccination.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 3, 203–8. [13 refs.]

Whenever serious complications follow BCG vaccination it is most important that the clinician and the bacteriologist should work closely together in order to elucidate the true role of BCG in causing such complications. Only thus can a true assessment be made of the risk.

A male infant aged 2 months, whose mother had inactive pulmonary tuberculosis, was vaccinated with fresh Danish BCG; there were no local complications. About 7 months after vaccination the child became ill and was found to have disease of the ulna. Surgical operation revealed an abscess from which pus was evacuated.

Culture of the pus gave many colonies of tubercle bacilli. The child was treated with isoniazid, and 3 months later there was complete healing with unimpaired mobility of the wrist joint.

Full details of the bacteriological methods used to identify the organism are given. It could not be distinguished from BCG by any of them. Examination of pathogenicity in guineapigs showed that the BCG strain and the patient's strain gave an almost identical picture after intracutaneous infection. No tuberculous changes could be seen macroscopically on autopsy of the guineapigs after 59 days. With subcutaneous and intraperitoneal infection no difference could be shown between BCG and the patient's strain.

It was concluded that although the methods available do not permit *certain* identification of the patient's strain with BCG the results were such that the only reasonable diagnosis is BCG. Such cases are very rare [see also this *Bulletin,* 1955, v. 30, 1019]. *H. G. Calwell*

BUONOMINI, G., DELLE SEDIE, P. F. & MENCACCI, G. F. **Tuberculin and Bacillary Allergy in Subjects vaccinated with Concentrated Petragnani Integral Anatuberculin (C.P.I.A.) by Multiple Skin Injections.** *Panminerva Med.* Turin. 1960, Nov., v. 2, No. 11, 549–51 2 figs. [Translated from Minerva Med., 1960, v. 51, 363.]

The vaccine used in this work was that known in Italy as "Anatuberculina Integrale Petragnani" which is prepared from cultures of various virulent strains of human, bovine and avian tubercle bacilli killed with formol [this *Bulletin,* 1955, v. 30, 118].

Only 512 of 1,723 children aged 5 to 16 years who had been vaccinated during the previous 5 years reacted to the patch test with concentrated and dried Petragnani Diagnostic Anatuberculin. This reactor rate of 29·7% was only twice that found in a group of children of the same age infected naturally during the period.

The authors therefore examined tuberculin sensitivity by means of the Mantoux and the bacillary tests in a group of vaccinated children. The Mantoux test was

performed with 20 TU of Anatuberculin, and the bacillary test was done by multiple puncture through a drop of the vaccine.

It was found that 32% of 225 vaccinated children who were negative to the patch test reacted to the Mantoux test, and 75% reacted to the bacillary test, a particularly marked reaction occurring in 56·3% of them. In 97 out of 225 the bacillary test was positive and the Mantoux negative.

The Mantoux and bacillary tests were also done in 164 unvaccinated children who did not react to the patch test. 15·5% were found to be Mantoux reactors and 13·2% showed marked bacillary allergy.

The authors do not consider the low post-vaccinal tuberculin conversion rate important since there was bacillary allergy in 85·2% of the total number of subjects. Allergy and immunity must be considered as distinct, and there is experimental evidence that tuberculin allergy due to vaccination appears later and disappears earlier than bacillary allergy, and that further resistance to tuberculous infection takes place after allergy and "infra-allergy" have disappeared. *H. G. Calwell*

JOINT TUBERCULOSIS COUNCIL. **Tuberculosis: Report on the Reception of Ex-Patients in respect of Re-Employment and Superannuation, Life Assurance and Emigration.** *Tubercle.* 1960, Oct., v. 41, No. 5, 370–79.

The Joint Tuberculosis Council seeks a "new deal" for ex-patients who have had pulmonary tuberculosis and their families in the matters of employment, life insurance and emigration. Facts and opinions concerning these problems were sought from chest physicians throughout the United Kingdom and 115 replies were received.

Regarding superannuation the majority replied that there was no major difficulty especially where it was a condition of the scheme that an interval of 10 years must elapse before benefits were payable. As a general rule the fact that a person has had a moderate degree of pulmonary tuberculosis adequately treated should not debar entry to a superannuation scheme.

Difficulty in getting employment or re-employment depended mainly on the amount of employment available in the area. It was, however, a general finding that government departments and local authorities were more reluctant to employ ex-patients than were many private employers.

What must be done is to give the widest publicity to the altered prognosis in all forms of tuberculosis. It is mentioned that some chest physicians are themselves not adequately aware of the improvement and are to blame for delaying the patient's return to work too long or prescribing light or part-time work without any medical necessity.

There has been considerable improvement as regards life insurance but some handicaps still exist. Most companies now accept on normal terms certain applicants with treated and inactive tuberculosis. There were however examples of severe loading only because of a history of family contact.

It appears that most of those concerned are aware of the improved prognosis with consequent improvement in conditions of acceptance of ex-patients and members of their families.

Agreement by the leading insurance companies on a common policy is desirable, and it is also important that some method be devised of informing companies without delay about changing opinions or experience regarding tuberculosis. Mortality tables, on which actuaries rely, may be out of date even before they are available for reference.

80% of those who replied about emigration problems gave instances of difficulty or hardship. They mentioned that it was very hard to obtain exact information about grounds for rejection. Immigration authorities are reluctant to disclose their reasons for delay or rejection.

Enquiries were made from the chief medical officers of the immigration departments of certain countries. Conditions are best illustrated by those prescribed by the U.S.A. which are given in detail. Canada appears to have even stricter requirements.

In view of the improvement in prognosis it is justifiable to ask whether this control is now too strict, is interpreted with unnecessary rigidity and pays too little heed to personal problems.

"It is hoped that the publication of this report may draw attention to the need for a new attitude towards pulmonary tuberculosis, so that advances in clinical treatment of this disease may be rewarded not only by clinical recovery but by greater acceptance of social and economic equality thereafter." *H. G. Calwell*

LEWIS, A. G., Jr., LASCHÉ, Eunice M., ARMSTRONG, A. L. & DUNBAR, F. P. **A Clinical Study of the Chronic Lung Disease due to Nonphotochromogenic Acid-Fast Bacilli.** *Ann. Intern. Med.* 1960, Aug., v. 53, No. 2, 273–85, 4 figs. [19 refs.]

Considerable interest has lately been aroused by the study of acid-fast bacilli capable of causing pulmonary disease which are not tubercle bacilli. This paper deals with Runyon's third group, non-photochromogens which the authors had divided into groups III–A (non-pigmented) and III–B (pigmented). They are both unaffected by light and are rapid growers.

The report describes 116 patients who had multiple isolations of non-photochromogens and who had completed a period of hospitalization in Florida. The characters of these bacilli are described. The search for other causative organisms in sputum, autopsy and surgical specimen was made in most cases. In 77 of the patients, cultures for fungi revealed only *Nocardia asteroides* in 1 instance and *Candida albicans* in a few cases. No other pathogens were discovered. Bacilli have been found in healthy individuals with normal chest X-rays. The disease occurs predominantly in white males over 40 years of age. In no instance did non-photochromogenic infection occur in more than one member of a family. Clinical symptoms in these patients were indistinguishable from those found in pulmonary tuberculosis. Cavitation occurred in 78% of patients; the radiological appearance of this disease could not be distinguished from that of tuberculosis. Pulmonary emphysema was thought to occur in 35 out of 116 patients. A table giving other associated diseases is given. Complete resistance to

isoniazid and PAS was almost invariably found. Treatment by the antimicrobials indicated by the resistance studies has been disappointing. 52·7% of the patients had not improved radiologically at discharge. In only 2 patients was cavity closure achieved without surgery. 43% of the discharged patients treated medically failed to attain sputum conversion. 37 patients had resection, and 1 an extraperiosteal plombage. Of these, 24 patients had a positive sputum at the start, and only 5 were positive on discharge. The complications of resection appeared to be higher than in a comparable group of tuberculous cases. 50 patients were discharged with active pulmonary disease, 17 patients died, 15 of whom had received medical treatment only. *F. H. Young*

VENEREAL DISEASES

KAROLY, I. Situation de la lutte antivénérienne en Hongrie, durant la période 1947–1957. [**The Venereal Diseases Campaign in Hungary 1947–1957**] *Santé Publique*. Bucharest. 1959, v. 2, Nos. 3/4, 307–23.

This very long article sets out the results of anti-venereal measures in Hungary over a 10-year period; it contains a mass of statistical detail for which the original should be consulted.

It suffices to say that during this period primary syphilis fell from 165·8 per 100,000 to 0·2, latent syphilis and secondary syphilis with complications from 207·1 to 35, gonorrhoea from 412·9 to 64·1 and chancroid from 18·4 to 0·2; the total figures were 804·2 and 99·9 respectively.

This success is largely due to anti-venereal dispensaries together with contact-tracing corps organized in the capital in 1953, and to the follow-up of syphilis cases; it is of interest to note that a large proportion of early syphilis occurs in rural districts, while a good deal is imported by seamen. Somewhat surprisingly, though latent syphilis fell slightly between 1953 and 1957, cardio-vascular, neuro- and congenital syphilis all rose; this last applied almost entirely to the 10–15 age-group.

More than 4 million prophylatic examinations were carried out in the 7 years 1951–1957 involving 41% of the population; most positive results were obtained in Budapest, followed in order by industrial and agricultural areas.

Serum tests employed included the Mandula, Kahn and VDRL and more recently the TPI; the opportunity for prophylatic testing included employment of workers, marriage, recruiting, pregnancy and hospital in- and out-patients.

Gonorrhoea patients fell from 22,726 in 1948 to 5,454 in 1957, men being affected approximately twice as often as women; women were the sources of infection in 90% of cases and those with chronic gonorrhoea constituted 75% of the total. Clandestine prostitution is considered responsible for most infections and to combat this police and social service action seems the most feasible.

[These facts are of considerable interest as coming from a country behind the Iron Curtain; one wonders if they are typical of others.] *T. E. Osmond*

DUMITRIU, R. Quelques aspects de l'action de prévention et de lutte contre la syphilis dans la République Populaire Roumaine. [**Some Aspects of the Prevention of and the Campaign against Syphilis in the Republic of Rumania**] *Santé Publique*. Bucharest. 1959, v. 2, Nos. 3/4, 325–30.

As in other countries the morbidity from syphilis reached its maximum in 1947, owing, among other things to the inferior status of women, prostitution, lack of a health organization and shortage of drugs. The suppression of prostitution and the setting up of health organizations (*circonscriptions sanitaries*) together with the provision of laboratories have helped in solving the problem; notification of syphilis cases has also helped. Treatment has been centred in clinics (*Centres—Dermato-Vénéréologiques*); this is obligatory and consists of a combination of penicillin, arsenic and bismuth, though arsenic has been dropped recently. Health education has also helped. For the unveiling of syphilis examination of pregnant women, pre-marriage tests and periodic anti-venereal control are employed.

During the period 1950–1957 the number of previously unknown cases of syphilis fell by 92%, the number of florid cases fell by 85%, that of neuro-syphilis by 83% and congenital syphilis has virtually disappeared; most of the fall occurred in the earlier years tailing off in 1956–1957; traced sources of infection rose from 46·2% in 1952 to 58·8% in 1957. In general, syphilis decreased in some towns but sporadic cases occurred in others forming reservoirs of infection; the fall in numbers was much more marked in rural than in urban localities. Where recrudescence occurred it was usually due to failure in contact tracing. *T. E. Osmond*

MAGATH, T. B. **The Serologic Problem of Syphilis, even Today.** *Amer. J. Clin. Path.* 1960, Oct., v. 34, No. 4, 338–45. [14 refs.]

This author is obviously a pessimist; his theme is to show that of all the serum tests for syphilis none are satisfactory or reliable. He quotes some 14 or so authors whose views on these tests vary from a moderate optimism to downright pessimism, and sets out a number of results obtained with various tests. In table 1 he compares the sensitivity and specificity rates of 11 tests (6 of which employed lipoid and 5 treponemal antigens); in table 2 he compares VDRL, Kolmer and Reiter complement-fixation (RPCF) tests whose sensitivity and specificity percentage rates were, respectively, 96·4 and 40, 81·5 and 61·1, and 64·1 and 90·1. In table 5 he shows that various tests with virulent treponemal antigens gave 10·6%, Reiter antigens 17·8% and lipoid antigens 14·5% false reactions.

Put briefly, no test or combination of tests can confirm or exclude syphilis; a positive treponemal test indicates high probability of syphilis but a negative one does not exclude it; a negative standard test (STS) is more likely

to be valid [in early syphilis] than a negative treponemal test; in late syphilis the TPI test is more often positive than STS and is likely to be more useful in assessing the results of treatment.

[The TPI test is generally thought to be more specific than STS but does not become positive so early; in many late cases of syphilis it tends to remain positive indefinitely and is therefore not of much value in determining whether treatment has been adequate or not. A test which will be 100% specific and 100% sensitive is obviously out of the question—no test is.]

T. E. Osmond

FAURE, M. & PILLOT, J., with the technical collaboration of F. AUTIN & J. MARÉCHAL. Composition antigénique des tréponèmes. III. L'antigène lipidique de Wassermann. [**Antigenic Constitution of *Treponema*. III. The Wassermann Lipidic Antigen**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 729–42. [30 refs.]

It is agreed that the Reiter treponeme contains the lipid antigen which reacts in the WR but there is not yet agreement about its immunological properties. The organism contains 20% lipids including lecithin and a phosphatid similar to cardiolipin which are not serologically very active.

These authors extracted the total lipids and submitted them to fractionation, and also prepared a protein extract. The Wassermann antigen contained in the organism is present in much larger amounts in the young spiral forms than in the older vesicular forms. In order to obtain a satisfactory antigen for the diagnosis of syphilis the titre of the group [protein] antigen should be much higher than that of lipid antigen; incidentally rabbits and guineapigs do not produce reagin when injected with Reiter treponemes. This article contains a good deal of technical detail for which the original should be consulted.

[If antigen can be produced which will react with the immune antibody contained in syphilitic serum but not with reagin the problem of biological false positive reactions should be solved.]

[See this *Bulletin*, 1960, v. 35, 993.] *T. E. Osmond*

VINCENT, D., BAZEX, A. & SALVADOR, R. Localisation électrophorétique de la réagine syphilitique par la méthode bidimensionnelle. [**Electrophoretic Localization of Syphilitic Reagin by the Bidimensional Method**] *C. R. Soc. Biol.* 1960, v. 154 No. 4, 820–22, 1 fig.

It is generally agreed that reagin is present in the globulins and more particularly the gamma globulins; according to LEGRAND (*Ann. de Biologie Clinique*, 1956, v. 14, 76) the Kolmer reaction is caused by gamma globulins and lipoproteins.

With the aid of a special apparatus serum treated by electrophoresis passes onto a vertical piece of paper flooded by a special solution with a *p*H of 8·6; this is submitted to an electrical field which causes the various fractions to spread out radially (as is well shown in a figure). The paper is then treated with bromophenol blue which shows up diverging bands of the various fractions which are collected into tubes.

The authors treated various fractions of positive syphilitic sera by means of the Kolmer Wassermann [? with lipoid antigen] and the Kline and VDRL slide tests with cardiolipin antigen. The separate fractions which gave closely comparable positive reactions with all 3 tests corresponded to a rather wide zone situated mostly just in front of the principal gamma globulin band; this zone included the " slow " beta globulins and the " rapid " gamma globulins.

Another zone was involved in anti-complementary reactions; this was situated just behind the positive zone.

T. E. Osmond

CHORPENNING, F. W. & BEERS, D. B. **The Effect of Added Calcium on Treponemal Immobilization.** *J. Immunology.* 1960, Sept., v. 85, No. 3, 240–43, 1 fig. [19 refs.]

It has been known for some time that an optimum level of calcium ion (Ca^{++}) has an enhancing effect on immune haemolysis and these authors thought that it might have the same action in immobilization reactions. They therefore carried out quantitative TPI reactions with and without added Ca^{++}; in the former was added 0·02 gm·$CaCl_2 \cdot 2H_2O$ per litre. Tests were carried out in the usual way with 5 two-fold parallel dilutions of a single antiserum pool; spirochaete antigen was adjusted to about 5 x 10^6 organisms per ml.; the volumes of complement were 0·04 and 0·08 ml. as determined by titration. In a series of tests the added Ca^{++} and the increased amounts of complement both separately and together resulted in higher titres; it was also noted that less haemolytic activity was lost in test mixtures to which Ca^{++} had been added. The explanation is not clear but the enhancing effect may have been due to a protective action of Ca^{++} on complement or to an essential requirement of Ca^{++} in the reaction; the optimal concentration of Ca^{++} is not known. *T. E. Osmond*

PETERSON, E. T., DE HAVEN, Roberta C., WRIGHT, E. T. & MILLER, J. N. **The Reiter Protein Complement-Fixation (RPCF) Test.** *Amer. J. Clin. Path.* 1960, Sept., v. 34, No. 3, 231–6.

The Reiter complement-fixation test (RPCF) was carried out on 479 sera from 215 patients, all of whom had given positive reactions with cardiolipin tests for syphilis; TPI tests were also performed. Cerebrospinal fluids from 39 patients were also tested by RPCF and Kolmer (cardiolipin) in parallel. With the sera RPCF and TPI agreed (both positive or both negative) in 165 (76·7%) of the patients; of the 50 where there was disagreement 24 were positive with RPCF and 26 positive with TPI. An analysis of results revealed no significant difference between the 2 tests as regards sensitivity or specificity. What did appear was that RPCF was not infrequently positive when repeated after the original result had been [apparently falsely] negative; it is concluded therefore that a positive RPCF indicates syphilis, past or present, but a negative reaction does not exclude it. Anti-complementary sera usually gave satisfactory results when treated by the modified Sachs method. In the case of 39 cerebrospinal fluids both RPCF and Kolmer tests

were positive in 25 but Kolmer alone was positive in 8 others, most of which were considered syphilitic; a repeat RPCF was positive in 2 out of 6 specimens which had been negative.

The authors think that some at least of the false negative RPCF tests were due to the presence of an inhibitor. *T. E. Osmond*

THIVOLET, J., GROSPIRON, D. & MURAT, M. Utilisation de l'immunofluorescence pour le diagnostic de la syphilis (note préliminaire). [**Immuno-Fluorescence in the Diagnosis of Syphilis; Preliminary Note**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1960, July–Aug., v. 8, No. 5, 501–9.

These authors employed a suspension of virulent spirochaetes, one drop of which was placed on a slide, dried and fixed by heat. Serum to be tested was heated at 56°C. Two kinds of marked fluorescent sera were used: (a) animal sera immunized against human globulins, and (b) human sera from syphilitic subjects with high-titre immobilizing antibodies. Conjugation was carried out with isothiocyanate of fluorescein. A special optical installation was used.

For technique (a) serum to be tested is allowed to act on the fixed spirochaetes and then a fluorescent animal anti-human-globulin serum is added; a positive result is indicated by fluorescence of the spirochaetes.

For technique (b) the test serum is allowed to act on the spirochaetes, and human syphilitic serum rendered fluorescent is then added; a positive result is indicated by absence of fluorescence in the spirochaetes.

With technique (a) results were not very satisfactory and special studies were carried out on antigen with trypsin, hyaluronidase and Versene [EDTA], on various dilutions of serum, on conjugates of fluorescent anti-globulins, and on time of contact (preferably 3 hours). The technique (b) is still under trial. Results of testing 143 sera in parallel by TPI, fluorescence, classical serum tests and treponema pallidum complement-fixation tests (TPCF) are given in a table. The number of positive results obtained with these tests were respectively 73, 88, 42 and 27 in syphilitic subjects; TPI and the fluorescence test gave no false positives, but classical tests gave 3 of these and TPCF 2. For full details of technique the original should be consulted. The authors consider their results encouraging but not yet definitive. Further research is necessary. *T. E. Osmond*

SMEDLEY, M. G. **Treatment of Gonorrhoea on the Far East Station.** *J. Roy. Nav. Med. Serv.* 1960, v. 45, No. 3, 119–24.

After commenting on the apparent resistance of gonococci to penicillin and quoting some results obtained by others [this *Bulletin*, 1958, v. 33, 654, 841; 1959, v. 34, 757] this author reports his experience in the Far East, where he treated 43 patients in a naval flotilla suffering from acute gonorrhoea on 3 different schedules, with the following results:

Singapore and Malaya: 13 cases 300,000 units PAM—2 failures; 8 cases 600,000 units PAM—3 failures; 14 cases 1 gm. streptomycin—2 failures. In Hong Kong penicillin dosages were doubled, and the figures were: 600,000 units—3 cases, 2 failures; 1,200,000 units—3 cases, 2 failures; streptomycin 1 gm.—2 cases, 1 failure.

Thus the overall penicillin failure rate for the Singapore-Malaya series works out at 23·8% which compares unfavourably with results obtained by MEAD *et al.* [see below].

For the future the author recommends 600,000 units of procaine penicillin and if this fails 1 gm. streptomycin [*ibid.*, 1960, v. 35, 464] plus a course of a sulphonamide. He appears to fear the masking of possible syphilis if relatively large doses of penicillin are employed [but surely these would cure an incubating syphilis out of hand].

[It is of interest to note that penicillin-resistant gonococci seem commoner in the Far East than elsewhere.] *T. E. Osmond*

MEAD, R. K., MOON, N. F. & BEAN, L. L. **Penicillin-Resistant Gonorrheal Urethritis in Male Personnel.** *U.S. Armed Forces Med. J.* 1960, Oct., v. 11, No. 10, 1117–23, 1 fig. [13 refs.]

There has been much discussion concerning penicillin-resistant gonococci in the last few years. These authors report 11 such cases (15·3% of all cases treated) occurring in a 6-month period.

The initial dosage in all cases of gonococcal urethritis was 600,000 units of procaine penicillin or more daily for 4 days. Of the 11 resistant cases, 4 were sensitive *in vitro*; in a table are also given results of sensitivity tests to other antibiotics.

Those patients who failed to be cured by the original dosage of penicillin were treated with [and presumably cured by] oxytetracycline 2 gm. x 10 and 1 gm. x 10, chloramphenicol 1 gm. x 7 (5 cases), erythromycin 2 gm. x 5, chloramphenicol 1 gm. x 6 and 1 gm. x 10; in addition 6 patients received sulphadiazine or sulphisoxazole as well.

The fact that all patients were military personnel kept under close observation almost certainly rules out reinfection; dosage certainly could not be considered inadequate. *T. E. Osmond*

BARR, F. S. & BRENT, B. J. **The Activity of Various Drugs against *Trichomonas vaginalis in vivo.*** *Antibiotics & Chemotherapy.* New York. 1960, Oct., v. 10, No. 10, 637–9.

"1. Solutions of tennecetin, glaucarubin, trichobisonium chloride, and nystatin were found to have trichomonacidal activity when tested *in vivo* subcutaneously in the ventral side of the mouse. The activity of acriflavine in this test confirmed previous experiments.

"2. Aqueous suspensions of griseofulvin and of nystatin were found to be inactive against *Trichomonas vaginalis.*

"3. Triacetin when used as an injection produced ulcers. We were, therefore, unable to reach a level high enough to determine the activity of the agent."

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

QUEENSLAND INST. OF MED. RES. **Fifteenth Annual Report of the Council of the Queensland Institute of Medical Research to the Honourable the Minister for Health and Home Affairs; Year ended 30th June, 1960.** 26 pp. 1960. Brisbane: S. G. Reid, Govt. Printer.

This report contains accounts of much scientific work. E. SINGER and G. M. J. RODDA write on mycobacteria of various groups from animals, dust, milk, or from human tonsils. They are evidently common, but though some of them may be able to cause disease in man, this has not been proved. M. F. RIDLEY reports on fungus diseases —*Microsporum gypseum* and *M. cookei* were isolated from rats and from soil—and I. COOKE and E. H. DERRICK discuss the high incidence of *Toxoplasma* antibodies found in various groups of patients and in domestic animals, though the organism has not yet been isolated from man in Australia, but has been seen in autopsy material.

Murine typhus is endemic round Toowoomba, and E. H. DERRICK and his colleagues comment on the rats and their fleas, and also on an outbreak of Q fever which may have originated by inhalation of dust or mud contaminated by bandicoots (known to be infected) or their parasites.

Murray Valley encephalitis virus, and dengue virus, infections were detected in serological surveys at various places, and R. L. DOHERTY and his colleagues found neutralizing antibodies to virus AMM 2354 in horses, cattle, pigs and possibly sheep, possums and ducks; sporadic human infection with this virus also occurred. 9 infectious agents have been isolated by intracerebral inoculation of mice with material from pools of *Culex annulirostris*; 5 were antigenically related to Murray Valley encephalitis virus. Enteroviruses and adenovirus were isolated from patients, and psittacosis virus from cockatoos, and unidentified agents from various animals.

Leptospire infection again attracted attention in bandicoots and rodents, especially from woodland, rain forest and sugarcane fields; J. L. HARRISON and M. L. EMANUEL report investigations on rodent populations and their movements. M. J. MACKERRAS reports a test in which bephenium hydroxynaphthoate gave much better results than tetrachloroethylene and hexyl resorcinol in hookworm infection. Various other parasitological and entomological investigations are also recorded and the report ends with a list of publications. It is a useful short account of the type of work done by this institute, and therefore, indirectly, of some of the important medical problems of the area. Almost all the work relates to the parasitic diseases. *Charles Wilcocks*

DUGDALE, A. E. & MCGEORGE, M. **Bronchiolitis in Infancy.** *New Zealand Med. J.* 1960, May, v. 59, No. 333, 227–36, 3 figs. [38 refs.]

This is an important paper on a topical subject—acute bronchiolitis in infancy. It is now being realized that many rapid respiratory deaths in infants attributed to broncho-pneumonia are more accurately described as due to bronchiolitis with obstructive emphysema and anoxia. The initial infection is generally held to be viral, although no particular virus specific for this condition has been demonstrated. The illness is often clinically mild at first, but severe distress may be alarmingly sudden and death occurs within 24 hours of onset of severe symptoms. This severe phase is due to respiratory obstruction from thickened bronchiolar walls and accumulation of mucus in these small tubes; this gives rise to hypoxia, as shown by respiratory distress, intercostal recession, restlessness, and finally cyanosis and collapse. There is little or no evidence of secondary bacterial infection in these infants; that tends to occur in older children with larger bronchial tubes.

The distinction between bronchiolitis and pneumonia is important in treatment. In this series of 21 infants with bronchiolitis the following treatment was found to be satisfactory. As a routine, oxygen with increased humidity was given along with a broad-spectrum antibiotic such as chloramphenicol to suppress invasive bacteria during the critical acute "viral phase". If the danger signals appeared, or seemed to be imminent—acute respiratory distress, hypoxia, intercostal retraction, restlessness, and finally cyanosis and collapse—steroid treatment was started at once and in large doses, and this was repeated if necessary until the distress finally abated. Hydrocortisone hemisuccinate 100 mgm. intramuscularly every 4 hours was actually used, and this was apparently life-saving in the 8 severe cases in the series.

H. Stanley Banks

FRY, J. **Fate of 424 Patients with Pneumonia and Bronchitis.** *Brit. Med. J.* 1960, Nov. 19, 1483–6.

The author, who practices in Kent, has become well known as a systematic compiler of records in his general practice, and a reviewer of the conditions met with in general practice and their progress over the years. He has now surveyed 424 of his patients who suffered from pneumonia or acute bronchitis in 1949–54, and has made an assessment of their condition in 1959—5 to 10 years later.

According to his method of grading (5 grades upwards from no disability requiring medical attention to death or complete invalidism) as many as 43% were considered to be disabled, including the 6% who had died and the 9% who were complete invalids. This rate of disability is more than twice that present before the respiratory infection 5–10 years earlier (21%). Lobar pneumonia had been present in 15%; in these the age incidence rose with increasing age, the sex incidence was equal, and the condition was most frequent in the lower social groups, in male smokers, and in those with a previous history of chest illness. Segmental pneumonia was most frequent in young children; the disability rate was 16% compared with 6% before the infection, and some correlation was

noted with social class and smoking. Acute bronchitis had an age incidence both in the young and the old. Disability at follow-up was present in 71%, compared with 38% before the infection; there were close associations with smoking, social class, and previous chest illnesses.

The burden of ill health reflected in these figures is apparent when one considers that a million persons in the United Kingdom are estimated to be affected annually by acute chest illness, with probable permanent disability in over 40%. Preventive measures must take into account the association between disability and age, sex, social class, smoking habits, past history, and environmental (*e.g.*, atmospheric pollution) and genetic influences.

H. Stanley Banks

GREENBERG, J. H., NADIG, P. W. & ROBERTS, D. L. **Outbreak in Unidentified Disease in American Personnel in Eritrea.** *U.S. Armed Forces Med. J.* 1960, Nov., v. 11, No. 11, 1263–75, 2 figs.

An epidemic disease, somewhat resembling infectious mononucleosis, broke out in November and December 1958 among U.S. military personnel and their civil dependents stationed in Asmara, Eritrea. During the previous year, gastro-enteritis and infective hepatitis had been unusually prevalent in this population, and one week before the appearance of the epidemic here described an explosive outbreak of acute pharyngitis had occurred. This was probably due to a streptococcal infection disseminated by food in a single mess hall.

The disease described began with fever and follicular tonsillitis, followed by the development of generalized lymphadenopathy and tenderness beneath both costal margins. No rash was seen. The blood showed an absolute lymphocytosis, but opinions differed as to the presence of atypical lymphocytes. The liver did not become palpably enlarged and jaundice did not develop, but in 5 patients out of 90 a palpable degree of splenomegaly was noted. The incubation period appeared to range from 3 to 23 days, averaging 8–9 days. The total duration of the illness is not noted, but the febrile phase was succeeded by a variable period of weakness and debility.

The earliest case was that of a schoolgirl, 16 years old, who owned a tame gazelle which had been ill with diarrhoea a few days before her disease began. Infectivity appeared to be high, for the disease affected mainly the older classes of schoolchildren who were in contact with the first case and with a teacher who was affected early in the epidemic, and the military hospital staff who nursed the patients.

The disease showed no complications and no sequelae, and recovery was complete and universal.

Laboratory facilities were very limited and there was no scope for attempts at isolation of a causal organism by culture or animal inoculation. Even the Paul-Bunnell reaction could not satisfactorily be carried out, as guinea-pig kidney absorption of the sera was not feasible.

[So very little information is available that speculation as to the aetiology of the condition is unprofitable. A *Listeria* infection of animal origin is suggested, but a viral agent is equally probable and even toxoplasmosis cannot be excluded.] *J. H. Walters*

BROWN, G. C. & KENDRICK, Pearl L. **Serologic Response of Infants to a Multiple Vaccine for Simultaneous Immunization against Diphtheria, Pertussis, Tetanus, and Poliomyelitis, in relation to the Presence of Specific Maternal Antibody.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1529–38. [26 refs.]

A study of Quadrigen, a prophylactic (made by Parke, Davis) containing poliomyelitis and pertussis vaccine and diphtheria and tetanus toxoids, in 48 children aged 2–4 months is reported. The infants received 3 doses at monthly intervals followed, for 31 infants, by a booster dose usually 6–8 months later. Sera were obtained before the start and 2 weeks after the primary and 3–4 weeks after the booster doses. (5 children only were bled just before boosting.)

Most children lacked maternal antibodies to diphtheria and tetanus and responded well to Quadrigen. However, only 2 out of 11 with pre-immunization levels of 0·1–1 unit of diphtheria antitoxin responded to the primary course and only 2 out of 5 who had tetanus antitoxin showed a response. The children who failed to make a detectable primary response still all had antibodies after a booster dose, implying some response because natural decay of antibodies should have caused a decline in the 6–8 months before a booster dose was given.

The response to pertussis was not good. 14 out of 43 children lacking maternal antibodies failed to produce pertussis agglutinins after the primary course but all of 26 tested responded to a booster dose. Few children had maternal antibodies, but those who did appeared to respond poorly to the booster as well as to the primary doses.

The response to poliomyelitis vaccine was also inhibited by maternal antibodies both for the primary and booster doses. Those without maternal antibodies responded better. 7 out of 18 showed a primary response to type 1 and 7 out of 8 (including 5 who failed to make a primary response) had antibodies after boosting. A similar pattern was seen for types 2 and 3 though the responses for these types were slightly better. Those with maternal antibodies had geometric mean titres of 24, 35 and 22 to types 1, 2 and 3, respectively, before vaccination and 4, 17 and 12 after boosting, whereas those without maternal antibodies had post booster geometric mean titres of 27, 161 and 268, respectively.

The authors conclude that serious consideration should be given to delaying immunization with poliomyelitis vaccine till maternal antibodies have declined to a low level. They suggest that it could still be combined with triple antigen. *A. J. Beale*

REIMANN, H. A. **Infectious Diseases. Twenty-Fifth Annual Review of Significant Publications.** *Arch. Intern. Med.* 1960, Nov., v. 106, No. 5, 679–713. [312 refs.]

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

EDWARDS, R. L. & GRESHAM, G. A. **Staphylococcal Pneumonia in the Neonatal Period.** *Lancet.* 1960, Nov. 12, 1057–8.

In this article, from the Department of Pathology of the University of Cambridge, 8 cases of fatal staphylococcal pneumonia in neonates are described. The infection was in most cases fulminant, and the strains of *Staphylococcus pyogenes* isolated in 5 cases were of the same antibiotic-resistance patterns as those isolated in the hospital; in 4 of these infants the route of infection was probably the maternal vagina, and 3 of them showed placentitis on histological examination.

The histological appearances in the infants' lungs were: in 2 cases intra-alveolar haemorrhage and necrosis with abundant staphylococci visible—evidence of fulminant infection with host resistances low; in 5 cases signs of bacterial bronchopneumonia with sparse intra-pulmonary haemorrhage—the duration of illness in these cases being days, rather than hours; in 1 case sparse polymorphonuclear leucocytic infiltration in the alveoli—the septicaemic type of lung lesion. The presence of numerous amniotic squames in the lungs of 6 of the infants suggested that the bronchopneumonia was due to inhalation of infected amniotic fluid; two infants were probably infected *post partum.*

The need for diligent application of aseptic methods in the care of the newly born, especially in hospital, is obvious. *H. Stanley Banks*

DUNNET, W. N. & SCHALLIBAUM, Evelyn M. **Scarlet-Fever-Like Illness due to Staphylococcal Infection.** *Lancet.* 1960, Dec. 3, 1227–9. [10 refs.]

The authors describe 3 cases of scarlet fever apparently caused by *Staphylococcus pyogenes.* [See also this *Bulletin,* 1943, v. 18, 8.] A filtrate prepared from one of the organisms contained an erythrogenic factor and an attempt was made, by carrying out tests on 37 patients not suffering from staphylococcal or streptococcal diseases and on 5 patients suffering from scarlet fever, to compare the filtrate with Dick toxin. Results were inconclusive but the authors feel that the staphylococcal erythrogenic toxin may differ in antigenic properties from Dick toxin.

A. B. Christie

MALESANI, S. M. Episodio familiare di reumatismo infettivo da streptococco Beta emolitico gruppo A. [**Family Outbreak of Infective Rheumatism due to Group A β-haemolytic Streptococci**] *Giorn. di Malattie Infettive e Parassit.* 1960, Aug., v. 12, No. 8, 436–8.

KEITH, J. D. **Modern Trends in Acute Rheumatic Fever.** *Canadian Med. Ass. J.* 1960, Oct. 8, v. 83, No. 15, 789–96, 7 figs. [28 refs.]

This is an excellent review of the incidence, diagnosis, and treatment of rheumatic fever in children.

The incidence has decreased in Canada from 2% of the school population 20 years ago to under 0·3% today. After streptococcal epidemics in young adults (especially service personnel) the incidence of rheumatic fever is relatively constant (3%); the corresponding figure for such epidemics among schoolchildren is estimated at about one-tenth of this (0·3%).

The major criteria for diagnosis are arthritis, carditis, nodules, chorea, and erythema marginatum; the minor criteria are fewer—raised erythrocyte sedimentation rate, lengthened conduction time, evidence of preceding streptococcal infection or a previous history of rheumatic fever. The functional heart murmur may cause difficulty. It is best heard towards the midline from the apex or at the left sternal border, is not propagated towards the axilla, is never heard throughout all systoles, and is usually maximal in mid-systole.

Recommendations for treatment are: (a) 1,200,000 units benzathine penicillin intramuscularly on 1st, 7th, and 14th day, and then monthly for 1 year [there is definite evidence that penicillin during the acute rheumatic attack is beneficial]; (b) aspirin 1–2 grains per pound daily for 3 months; (c) prednisone 15 mgm. every 6 hours daily for the first week, decreasing to 2·5 mgm. twice daily on the 14th day. Steroid treatment at the beginning of an acute attack makes the nodules, heart murmurs, and abnormal conduction time disappear more rapidly than when salicylate therapy alone is used.

For prophylaxis, benzathine penicillin 1,200,000 units monthly is undoubtedly the best; oral penicillin in equivalent dosage (2 tablets daily) is very expensive. Sulphonamide prophylaxis (1 grain daily over 60 lb. weight) is reasonably satisfactory, but will not clear streptococci from an infected throat.

Prognosis is dealt with in the report of the co-operative trial (see below). *H. Stanley Banks*

MEDICAL RES. COUNCIL: AMERICAN HEART ASS. **Evolution of Rheumatic Heart Disease in Children. Five-Year Report of a Co-operative Clinical Trial of A.C.T.H., Cortisone, and Aspirin. A Joint Report by the Rheumatic Fever Working Party of the Medical Research Council of Great Britain and the Subcommittee of Principal Investigators of the American Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association.** *Brit. Med. J.* 1960, Oct. 8, 1033–9. [11 refs.] [Also in *Canadian Med. Ass. J.* 1960, Oct. 8, v. 83, No. 15, 781–9, & *Circulation.* New York. 1960, Oct., v. 22, No. 4, Pt. 1, 503–15.]

This controlled cooperative clinical trial was set up in 1951–52, and a previous report [this *Bulletin,* 1955, v. 30, 868] compared the three treatment groups of 497 cases in detail throughout the 6 weeks of treatment, 3 succeeding weeks of observation, and a follow-up at the end of a further year; at this follow-up no significant difference between the 3 treatment groups was found in the status of the heart. Of the 497 children, 445 (89·5%) were

followed up for 5 years; only 16 (3·2%) died, 14 from rheumatic heart disease—a strikingly low fatality rate—and 36 were untraced. The present report confirms the previous findings (at 1 year); there was no evidence that the prognosis had been influenced more by one treatment than by another.

The major factor in prognosis is the status of the heart when treatment is begun. For patients without carditis initially there was no residual heart disease in 96% after 5 years' observation. For those with carditis initially, but without pre-existing heart disease, the proportion without residual heart disease after 5 years decreased from 82% where there had been only a grade I apical systolic murmur to 30% where there had been heart failure or pericarditis; and in this category where recurrences had taken place, the proportion with cardiac murmurs was higher. *H. Stanley Banks*

BUNN, P. A. & KNIGHT, Ruth. **Treatment of Pneumococcal Pneumonia with a New Penicillin: Clinical Observations in 25 Patients.** *Amer. J. Med. Sci.* 1960, Aug., v. 240, No. 2, 192–6.

Penicillin still remains the treatment of choice for pneumococcal pneumonia, except in penicillin-sensitive subjects. The new penicillin tried here in 25 adult patients, ranging in age from 18 to 86, was potassium alpha-phenoxyethyl penicillin (Syncillin) given orally. In its preparation the chemical side chain is added synthetically to the penicillin nucleus 6-amino penicillanic acid obtained by fermentation. Although all were acute severe cases, complicated in 10 by associated diseases, the results were excellent in all; in the older patients, as was expected, resolution was slower than in the younger. The dosage used in the last 11 of the group, 250 mgm. 3 times daily, was perfectly satisfactory. It produced a serum concentration above 0·05 μgm. per ml. for at least 4 hours after each dose; as the recovery phase of the growth of the organisms following cessation of exposure to penicillin does not recommence for at least 6 hours, this regimen was considered adequate, and proved to be so in the series. *H. Stanley Banks.*

FINLAND, M. **Shattuck Lecture. Treatment of Pneumonia and other Serious Infections.** *New England J. of Med.* 1960, Aug. 4, v. 263, No. 5, 207–21, 5 figs. [28 refs.]

This is a historical review of the treatment of pneumonia, and of serious infections due to the haemolytic streptococcus, *Staphylococcus aureus*, *Streptococcus viridans*, enterococcus, *Escherichia coli*, *Proteus*, *Pseudomonas pyocyanea* and *Aerobacter aerogenes* from 1935 onwards. The key years 1935, 1941, 1947, 1951, 1953, 1955, and 1957 are chosen to represent periods when new chemotherapeutic agents were introduced. Tables and figures show the numbers of patients treated, the number and percentage of deaths, percentage of total patients, and percentage of total deaths for each of these years. A continuing picture is thus presented of the effects of the introduction of sulphanilamide, the major sulphonamides, penicillin and streptomycin, the broad-spectrum antibiotics, and the new antibiotics since 1955.

Two factors leading to relatively high mortality in all these infections are (1) positive blood culture, and (2) age under 2 years or (increasingly) over 40. The darker side of the picture is that blood stream invasion by the four common coliform organisms, *E. coli*, *Proteus*, *Ps. pyocyanea*, and *A. aerogenes*, as well as that due to enterococci, has increased markedly since the introduction of modern antimicrobial drugs. From these 5 infections there was, in this series, a 6-fold increase in the number of patients, and a 7-fold increase in the number of deaths. The mortality in these cases has always been high and has increased from 40% to 50%. They now give rise to about half the deaths among bacteriaemic patients. The brighter side of the picture is, of course, the immense reduction of morbidity and mortality from the infectious diseases. The bacteria that were the most important causes of severe infection and mortality have been reduced to a minor role, whereas those that were infrequent causes of bacteriaemia before 1935 are now responsible for a very high proportion of bacteriaemic infections and most of the deaths (if we include under this heading *Staph. aureus* as well as the normal enterobacteria and others).

The causes of this disappointing state of affairs are complex, but include the almost universal resort to antimicrobial agents, increasing laxity in applying aseptic techniques for avoiding infection and cross-infection, and the ageing population. It is sobering to reflect that early successes with the antibiotics eventually leave residuals that become increasingly difficult to manage.

H. Stanley Banks

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

SALAMANDRA, R. Considerazioni sul recente andamento della difterite nel Comune di Grosseto. **[Observations on the Recent Course of Diphtheria in the Commune of Grosseto]** *Giorn. di Malattie Infettive e Parassit.* 1960, July, v. 12, No. 7, 344–8, 3 graphs. [17 refs.]

The author gives details covering the ten-year period January 1, 1948 to December 31,1957 regarding population and notifications of diphtheria, the figures being obtained from the Health Department of this Tuscan commune. During the period the population rose from 35,405 to

46,510 and while the number of cases of diphtheria notified was never more than 5 till 1955, from then on the figures were 26, 64, and 26 respectively, the total for the 10 years being 143.

The sexes were almost equally attacked except in 1955 when males predominated; the age-groups most affected were the 0–5 and for the last 3 years the 6–10 group also. There was an epidemic [not described in detail] in 1956 when 4 cases occurred in the 31–40 group. Only 6 deaths in all took place, all except 1 in the last 3 years. Most cases occurred in the autumn, especially in November.

80 cases occurred in persons stated to have been vaccinated, 63 in non-vaccinated. In the former group none had had a booster dose and only 65 had been properly vaccinated. However, the author taking a period of 5 years after vaccination as being still valid for immunity in this way excluded 46 of the 65; thus only 19 cases occurred among persons with some presumable immunity.

In discussing this the author points out the spread in the last few years to older children and suggests that apart from vaccination, improved hygienic conditions have led to less diffusion of the organisms and so to a lower incidence of inapparent infections. He points out that the vaccination state of the commune is probably better than many other areas in Italy so that possibly the increase may be attributable to a deficient natural immunity in the population; he rejects the possibility of strains of increased toxicity, and also that of lack of artificial immunity.

[This paper leaves so much unexplained that it is impossible to give a reasoned criticism. 3 deaths out of 26 cases occurred in 1955 and only 2 out of 65 in 1956. No details are given of either the clinical or bacteriological facts, or of the 1956 epidemic. On the face of it this rather suggests the arrival of a more virulent strain.]

W. K. Dunscombe

Pejak-Grbac, O. O jednom žarištu maligne difterije u Moslavini. [**A Focus of Malignant Diphtheria in Moslavina**] *Higijena.* Belgrade. 1960, v. 12, No. 1, 83–90, 1 fig. [11 refs.] English summary (9 lines).

The author describes a small outbreak of diphtheria occurring in a village in Yugoslavia in 1957, in which a carrier gave rise to 3 cases. The first patient was a boy aged 4, who died; his brother, aged 2, developed the disease 9 days later and recovered after treatment in hospital for 53 days. The third was a girl aged 5 who was the cousin of the first 2 patients; she lived in a house some way off but had frequent contact with them. Her illness began 22 days after that of the second patient, and from the length of the interval it was concluded that the infection had been derived from a carrier. *Corynebacterium diphtheriae* type *gravis* could be isolated from the 3 patients; examination of preschool and schoolchildren living in the village was negative, but organisms of the same type were isolated from the mother of the first 2 patients and from their 6-year-old sister. The mother was still a carrier when examined 15 months later.

D. J. Bauer

Biersteker, K. & Voors, A. W. **An Epidemic in Netherlands New Guinea.** *Papua & New Guinea Med. J.* Port Moresby. 1960, Apr., v. 4, No. 1, 34–40, 1 fig.

A sudden epidemic with a high morbidity (about 50%) and a high fatality rate in severe cases (about 50%) occurred among a primitive people living in small villages. Only a few serious cases were under medical observation. The clinical features were: (1) short incubation period, (2) sore throat and collar-like submandibular oedema, (3) foul breath with diphtheria-like odour, (4) difficulty in speech and swallowing, (5) fatal in a few days, (6) paretic legs in convalescents. Throat swab cultures examined after 5 days were " crowded with typical diphtheria rods ". Schick test surveys in a few villages showed a low percentage of positives after 5 years of age.

The authors speculate that this was diphtheria of Waterhouse-Friderichsen type, with loss of immunity due to malnutrition. [The observations are few and of poor quality, but it would seem more likely that the epidemic was due to invasion of the district by a highly virulent *Corynebacterium diphtheriae*, probably of *gravis* type, producing a high proportion of malignant " bull-neck " cases. Further outbreaks are likely, gradually becoming milder as herd immunity to the strain increases.]

H. Stanley Banks

Uttley, K. H. **The Epidemiology and Mortality of Whooping Cough in the Negro over the last Hundred Years in Antigua, British West Indies.** *West Indian Med. J.* 1960, June, v. 9, No. 2, 77–95. [12 refs.]

The death rates for whooping cough have been found for the 10 decennial periods from 1857. The usual pattern of a higher female mortality than male was found except during 1917–26 and 1927–36 when the male rate was 50% larger than the female. The mortality from whooping cough under age 15 was similar in Antigua and England and Wales until the turn of the present century. The death rate started to fall in England and Wales at the turn of the century and is now about one-fortieth of the initial level; in Antigua the fall in mortality did not begin until the mid 1920s and the rate is now about one-quarter of its original level. The consequence of this differential fall is that the mortality from whooping cough in Antigua is now almost 10 times that of England and Wales.

During the 100 years reviewed the deaths from whooping cough formed 1–2% of the total deaths. Of the 1,178 deaths recorded 539 were of males, 681 were of infants under 1 year of age and 444 were of children aged 1–4 years. Although the climate of Antigua does not vary much throughout the year there was a marked seasonal distribution of deaths in the early period. During 1857–93 56% of the deaths occurred in the third quarter and only 2% in the first quarter; after this period deaths occurred fairly evenly in each quarter with the rate for the third quarter slightly below the rate of the other quarters. The change in the seasonal distribution of deaths was accompanied by a slight change in the age distribution with a shift to the younger age-group.

W. J. Martin

TOMASIC, P. & GRAU, A. Fagotipizacija sa osvrtom na tifusne epidemije u Osijeku i okolini. **[Phage-typing and some Comments on Epidemics of Typhoid Fever in Osijek and its Environs]** *Higijena.* Belgrade. 1960, v. 12, No. 1, 26–34, 7 figs. English summary (7 lines).

Type A was the phage type most frequently encountered among 419 strains of *Salmonella typhi* isolated in 1954–58 in the town and environs of Osijek, Yugoslavia, representing from 14·59 to 51·21% of the total number of strains isolated in different years. The frequency of type C ranged from 1·63 to 19·25%, type D_1 from 4·87 to 23·95, type E_1 from 3·84 to 35·29% and type F_1 from 4·68 to 12·82; 8 strains were untypable and 14 were Vi-negative. A number of epidemics of typhoid which occurred in the area are briefly described. *D. J. Bauer*

UTTLEY, K. H. **The Mortality and Epidemiology of Typhoid Fever in the Coloured Inhabitants of Antigua, West Indies, over the last Hundred Years.** *West Indian Med. J.* 1960, June, v. 9, No. 2, 114–23. [14 refs.]

During the 100 years 1857–1956 known deaths from typhoid fever numbered 431. Excluding the early years for which the data are unreliable the death rate has varied between 9 and 25 per 100,000 in the 7 decennial periods. The male mortality exceeded that of the females, particularly at ages over 35 years. There was very little seasonal variation in the death rate although the mortality was highest in the third and fourth quarters, the period of greatest rainfall. The age distribution of deaths was constant throughout the period. The maximum mortality occurred at ages 20–24 years for both sexes, a secondary maximum occurred for males in old age but the rate for females fell steadily from ages 20–24 onwards.
W. J. Martin

FALISEVAC, J. & PADLEY, R. **An Outbreak of Typhoid Fever in the Warakapola Area of Ceylon February–July 1958.** *Trans. Soc. Med. Officers of Health, Ceylon.* 1959, Sept., v. 18, 39–51.

The authors, an epidemiologist and a statistician visiting Ceylon on behalf of WHO, discovered an outbreak of 25 cases of typhoid fever in a primitive rural village; these were linked to an earlier unrecorded outbreak of 8 cases, making 33 cases arising in 10 households comprising 67 persons. This high clinical attack rate suggests that the principal mode of spread was by direct contact, or dirty hands, rather than by infected water, which usually involves a much smaller proportion of the population at risk. Other factors supporting this hypothesis were; (1) the attack rate in households of more than 8 persons was more than twice that in smaller households, and (2) the younger males (under 25 years) and women of all ages were attacked much more frequently than the older males.

The epidemiological situation seemed to be that an endemic chain of infection had been smouldering for years in carriers and individual mild cases, with occasional flare-up of small outbreaks such as the one recorded here. The continuing infection was thought to be helped by the use of chloramphenicol in hospital patients, leading to early discharge as soon as the patients were afebrile and without the precaution of release cultures; thus 20 out of the 23 patients treated in hospital were discharged after 15 days or less, and among these 8 relapses were observed after they had returned home. [It is to be hoped that the local health authorities in Ceylon profited from these enlightening and helpful observations of the WHO representatives.] *H. Stanley Banks*

BHANDARI, N. R. & POHOWALLA, J. N. **Some Observations on Typhoid Encephalopathy in Children.** *Indian J. Child Health.* 1960, Aug., v. 9, No. 8, 375–9.

This is the third paper from the Indore school, represented by J. N. Pohowalla, on a syndrome in typhoid fever in children which they have termed "typhoid encephalopathy." The main symptoms appear to be convulsions, coma or semi-coma, and a stuporose state persisting for a variable period after subsidence of the temperature; these can be combined with absent abdominal reflexes and extensor planter responses (rather difficult signs to evaluate in children). Meningism or meningitis is not a part of this syndrome. This would seem to be a new name for what has previously been called the toxic nervous complications of the disease.

In a series of 450 child patients with typhoid (a rich experience which has not been available to western observers for at least two generations) the authors picked out 38 (8·4%) who exhibited this syndrome, and had a fatality rate of 28·9% compared with the overall fatality rate of 9·1% in the series as a whole. From previous work they had expected to find a beneficial effect from corticosteroid treatment of this syndrome, but this hope was not realized. An allergic basis for the syndrome does not appear to be likely, and the only distinctive finding is that the prognosis is poor, especially in children under 3 years of age with convulsions or coma. But there is surely nothing new in that. *H. Stanley Banks*

BEEUWKES, H., MOUTON, R. P. & DURLINGER, L. **A Study of the Influence of Polymyxin combined with Chloramphenicol on *Salmonella in vitro* and *in vivo* in Carriers of *S. paratyphi B.*** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 3, 340–48.

Other authors [MANTEN and DE NOOY, this *Bulletin*, 1960, v. 35, 282] have reported that polymyxin and chloramphenicol act synergically on *Salmonella typhi*, and suggested that this combination might be tried in carriers. The present authors, using a different method (discs and replica plating) have observed a similar effect of this combination on *Salm. paratyphi B* and *Salm. typhi-murium.* An epidemic of paratyphoid B in nurses and servants gave them the opportunity for a clinical trial: 12 servants and 30 nurses with positive stools were divided into 3 groups given respectively chloramphenicol and polymyxin, polymyxin only, each for 1 week, and no treatment. There was apparently no evidence of any effect; 9 out of 14 of those treated with the combination

were still positive after the course. No details are given of the duration of the carrier state, except in the statement that the experiment was carried out "immediately after the outbreak occurred". *L. P. Garrod*

PALMISANO, C. Considerazioni cliniche e terapeutiche su 466 casi di Salmonellosi (da *Salmonella typhi murium*) nell'età infantile, trattati con l'associazione chemioantibiotica + analettici cardio-respiratori e corteccia surrenale. **[Clinical and Therapeutic Observations on 466 Cases of *Salm. typhi-murium* Infection in Children treated by Chemotherapeutic Agents, Antibiotics, Respiratory and Heart Stimulants, and Suprarenal Cortical Extracts]** *Giorn. di Malattie Infettive e Parassit.* 1960, May–June, v. 12, Nos. 5/6, 285–7.

In July–August 1958, 466 out of 815 children in a summer camp suffered from *Salmonella typhi-murium* infection. On the basis of their temperature curve cases could be classified in 3 groups: (1) very acute gastro-enteritis with a high temperature; (2) acute febrile gastro-enteritis with a dysenteric, toxaemic syndrome and pseudo-appendicular manifestations; (3) mild, sub-febrile enterocolitis. The peculiarities of the disease in children appear to be the sharp, sudden onset and the abdominal symptoms with pain at MacBurney's point simulating appendicitis. Intoxication was severe, producing dehydration, reducing the alkaline reserve and bringing about acidosis, which often went on to a depletion of the blood electrolytes and to circulatory insufficiency.

Treatment was based on the use of chloramphenicol, neomycin and bacitracin, the use of deoxycorticosterones with vitamin C, the use as cardio-respiratory stimulants of the dimethyl-amide of N crotonil-α-ethylamine butyric acid and α-propylamino butyric acid and of electrolyte solutions consisting of sodium lactate. The stimulant was given as the preparation Micoren, 1 to 2 phials of which were given parenterally in the very acute cases 2 to 3 times daily in children between 6 and 8 years, while two-thirds of a phial were given to children between 10 and 12. In the patients with a pseudo-appendicular syndrome, treatment was kept up after the acute phase by the oral administration of 6 to 8 drops of Micoren 2 to 3 times a day in children between 6 and 8. The author attributes a great importance to the use of this drug. None of the patients died.

No reference is made to the epidemiology of this extensive outbreak. *E. Agius*

ROSSI, G. & ANDREONI, O. Considerazioni cliniche e rilievi anatomo-patologici in 4 casi mortali di affezioni acute da *S. typhi murium*. **[Clinical and Pathological Features in 4 Fatal Cases of Acute *Salmonella typhi-murium* Infection]** *Giorn. di Malattie Infettive e Parassit.* 1960, Aug., v. 12, No. 8, 385–9, 9 figs.

GOODWIN, M. H., Jr., MACKEL, D. C., GANELIN, R. S., WEAVER, R. E. & PAYNE, F. J. **Observation on Etiology of Diarrheal Diseases in Arizona.** *Amer. J. Trop. Med. & Hyg.* 1960, May, v. 9, No. 3, 336–42.

In this report more than two-thirds of the 630 persons in the investigation were infants of less than 1 year of age. Pathogenic bacteria were isolated from 57% of the total as a result of a single examination of the stools. Shigellae were isolated from 26%, entero-pathogenic *Escherichia coli* from 31% and salmonellae from 7%. About 90% of all the entero-pathogenic *E. coli* recovered came from young infants and about 40% of the shigellae came from the same group. Earlier studies in the South-west of the U.S.A. [this *Bulletin*, 1945, v. 20, 663] showed a higher incidence of shigella infections with more persons in age-groups above one year. Whether these different results reflect a changing epidemiological pattern or not is uncertain from the information made available. Although the peak incidence of the shigella infections was in the 2–12 year age-group, as would be expected, it is of interest to note that the majority of these were due to *Sh. flexneri*; only about 15% were due to *Sh. sonnei*. *H. J. Bensted*

IPPOLITO, A., DE SANTIS, R., CICCONETTI, G. & MANNO, G. Fenomeno di "prozona" ed anticorpi incompleti nella sierologia della infezione brucellare. **[On the Prozone Phenomenon and the Existence of Incomplete Antibodies in the Serology of *Brucella* Infections]** *Riv. Istituto Sieroterap. Ital.* 1960, May–June, v. 35, No. 3, 404–16. [16 refs.] English summary (7 lines).

The absence of agglutination of *Brucella* suspensions in high concentrations of antisera which are capable of agglutinating the bacteria when more diluted—the prozone phenomenon—has been attributed to coating of the bacterial cell by globulin which is only a partly developed or incomplete antibody. It has been observed that agglutination takes place in the tubes showing this phenomenon if Coombs antiserum for human globulin is added.

The authors readily confirm this observation but they reject the theory of incomplete antibodies. Their grounds for so doing are that this susceptibility to agglutination by Coombs serum is shown equally by *Brucella* suspensions previously exposed to anti-typhoid serum, by *Salmonella typhi* suspensions exposed to *Brucella* serum and by *Brucella* suspensions exposed to human serum in which the balance of globulins is abnormal, but does not occur after exposure to serum normal in its protein composition. That is to say, it is a phenomenon due in all probability to coating of the bacteria with globulin, but a non-specific one. If a *Brucella* suspension is treated with an adequate dilution of anti-*Brucella* serum and spun down after 90 minutes and resuspended in 0·85% NaCl solution, it agglutinates frankly. If resuspended in the supernatant from a tube of the prozone group in a brucella agglutination they fail to agglutinate or agglutinate very weakly, *i.e.* the interference is with the second phase, according to BORDET, of the phenomenon of agglutination. *J. W. McLeod*

FLAMM, H. & WIEDERMANN, G. Zur Methodik der serologischen Tularämie-Diagnositk. **[The Technique of Serological Diagnosis of Tularaemia]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 2, 254–63.

The work recorded was undertaken on account of the experience of a large but localized epidemic of tularaemia in a sugar refinery in Austria.

With a commercial diagnostic antigen of *Brucella tularensis* all the sera at first received from the patients in this epidemic were negative in macroscopic tube agglutination tests. Later sera were received which gave high positive titres although parallel tests with the sera received earlier remained negative.

It was found, however, that the use of much more concentrated antigen suspensions gave positive tests with the sera obtained earlier and the suspensions of bacteria separated after exposure of the more dilute antigens to the sera were agglutinated by Coombs antiserum to human globulin.

The authors conclude that these sera which had given negative results did so on account of considerable content of incomplete antibodies which were eliminated in presence of the heavier antigen suspensions.

With a view to obtaining rapid and sharp results and eliminating misleading findings due to incomplete antibodies such as they had experienced, the authors recommend the use of heavy bacterial suspensions killed by exposure to 0·5% phenol and combined with particulate suspensions of latex (Bacto-Latex of particle diameter 0·81μ of Difco Laboratories, Detroit). 0·1 ml. of latex is added to 0·4–2·0 ml. of bacterial suspension of suitable concentration and suspended in 10 ml. of Bacto RA buffer.

Latex and buffer suspension keep almost indefinitely and the bacterial suspension at least two months in refrigerator. *J. W. McLeod*

Vega Núñez, J. Pústula maligna. Estudio de 23 casos en la Ciudad de Morelia. **[Malignant Pustule. Study of 23 cases in the city of Morelia]** *Dermatologia.* Mexico. 1960, Mar., v. 4, No. 1, 4–19, 14 figs. [17 refs.] English summary.

This is a clinical description of 23 cases of cutaneous anthrax observed and treated by the author in the course of 3 years. He dislikes the term "malignant pustule" as it leads to confusion with other skin lesions not caused by *Bacillus anthracis*. Transmission in most cases was by contact with animals, a few followed insect bites. In one case, a woman had anthrax sores on the fingers and a week later her child, aged one year, developed anthrax on the elbow. All the patients, except one who died in diabetic coma, were successfully treated with antibiotics, the commonest being a combination of penicillin and streptomycin. The article is well illustrated.

A. B. Christie

Patel, J. C., Mehta, B. C., Dhirawani, M. K. & Trivedi, Rajni R. **Tetanus Neonatorum.** *Indian J. Child Health.* 1960, Oct., v. 9, No. 10, 459–68, 2 graphs & 1 map. [17 refs.]

During the 4 year period, November 1, 1954 to October 31, 1958, 308 cases of tetanus neonatorum were admitted to the King Edward Memorial Hospital, Bombay. [This bald figure indicates the magnitude of this public health problem in urban India.] The present report concerns 292 of these patients, the remainder having been removed prematurely from hospital.

Routine management comprised an initial injection of atropine 1/400 grain and adrenalin 1/8 ml. of a 1/1000 solution, followed 30 minutes later by an intramuscular injection of 20,000 units of antitetanic serum. Crystalline penicillin G, 0·5 mega unit, was injected twice daily and sedation was achieved by the use of paraldehyde by intramuscular injection. Cortisone was added to the above therapy during the last year of the study period.

The overall mortality rate in this neonatal series was 88·4%. Septic infection of the umbilical stump did not seem to influence the prognosis, while delay in the administration of serum did not seem to do so either, though this inference is probably fallacious since delay was maximal in the mildest patients, who tended to be brought later to hospital than those more seriously affected. The series bore out the well-recognized facts that the longer the incubation period, and the slower the development of symptoms, the better is the prognosis. The commonest presenting sign was inability to suck, while in some instances tetanic spasms were the first sign noticed. Death commonly occurred from laryngeal spasm, hyperpyrexia, or pulmonary oedema.

The authors admit that intramuscular paraldehyde is not an ideal sedative in tetanus [but did not employ chlorpromazine as an alternative]. Steroid therapy did not appear to improve the prognosis. *J. H. Walters*

Aguileiro Moreira, J. M., Brañeiro, R. L. & Ghigliazza, H. M. Segundo ataque clínico de tétanos. A propósito de una observación. **[A Case of a Second Tetanic Clinical Attack]** *Semana Méd.* 1960, Sept. 19, v. 117, No. 25, 969–76. [12 refs.] English summary.

A male patient aged 49 was treated for tetanus in the Infectious Diseases Hospital, Buenos Aires, in 1957. 4½ years previously he had been treated in the same ward for the same disease. On each occasion the attack seems to have been a fairly severe one. He had a chronic ulcer of the left leg which may have been the source of infection with tetanus on each occasion. The author emphasizes the fact that immunity does not follow a clinical attack and that patients on recovery should be actively immunized against the disease. *A. B. Christie*

Patel, J. C., Aiyar, A. A., Mehta, B. C. & Nanavati, B. H. **Dosage of Antitetanus Serum in the Treatment of Tetanus.** *Indian J. Med. Sci.* 1960, Oct., v. 14, No. 10, 855–60, 1 fig.

The authors treated 3 successive groups of patients suffering from tetanus with 20,000, 10,000, and 5,000 units of tetanus antitoxin: there were 219 patients in the first group, 347 in the second and 392 in the third. Patients were grouped into 5 groups according to clinical severity. Dosage did not affect mortality rate, which appeared to be related only to clinical severity.

The authors compared these results with others published earlier [this *Bulletin*, 1959, v. 34, 627; 1960, v. 35, 267] where the dosage had been 60,000 and 120,000 units: the mortality rate was *higher* with these doses.

62 patients were treated without antitoxin: the authors claim that in patients in grades of severity 3, 4 and 5 the mortality was greater than in those treated with low

doses, but do not point out that in grades 1, 2 and 3 the mortality for the untreated is lower than for those treated with high doses.

[Only if groups of patients were treated concurrently with differing doses could valid results be expected. As far as one can make deductions from the results given, it seems clear that clinical severity is much more closely related to mortality than dosage of antitoxin.]

A. B. Christie

BUFF, B. H. **Fatal Anaphylactic Shock, following Intradermal Skin Test with Dilute Horse Serum Tetanus Antitoxin.** *J. Amer. Med. Ass.* 1960, Oct. 29, v. 174, No. 9, 1200–201. [12 refs.]

A man aged 59 given an intradermal injection of 0·1 ml. of a 1 in 10 dilution of tetanus antitoxin died an hour later from anaphylactic shock in spite of treatment with epinephrine and hydrocortisone and the passing of a Chevalier Jackson tube into the trachea followed by oxygen under positive pressure. He had no history of having previously been injected with horse serum nor any history of allergy other than a skin rash following penicillin.

A. B. Christie

GODFREY, M. P., PARSONS, V. & RAWSTRON, J. R. **Rapid Destruction of Antitetanus Serum in a Patient previously sensitised to Horse Serum.** *Lancet.* 1960, Dec. 3, 1229–30.

A patient suffering from a compound fracture of tibia and fibula was given 1,500 units of tetanus antitoxin. 6 months later the wound was still discharging and symptoms of tetanus developed: subcutaneous test doses of 0·2 ml. and 1·0 ml. were followed by a 2 cm. area of local erythema. After 6 ml. had been given he developed anaphylactic shock.

The patient eventually recovered from his illness and estimations of serum antitoxin and of antibody to horse serum and to tetanus antitoxin were carried out. These showed that antitoxin was rapidly eliminated: at the 6th day only half the expected amount was present and at the 9th day all the antitoxin had been eliminated. By contrast, antibodies to horse serum and to horse tetanus antitoxin were high by the 9th day and were still detectable after 6 months. Antibodies to sheep, pig and goat serum were also present though in much lower titre. The article emphasizes the fact that, in patients who have previously had an injection of horse serum, antitoxin may be very rapidly eliminated and protection very short-lived.

A. B. Christie

FILLER, R. M. & ELLERBECK, W. **Tetanus Prophylaxis.** *J. Amer. Med. Ass.* 1960, Sept. 3, v. 174, No. 1, 1–4, 1 graph. [19 refs.]

Clinical tetanus is rare but the case-mortality rate is high. Because of the limitations of tetanus antitoxin as a prophylactic in the treatment of wounds, the ease with which active immunity can be induced with fluid or alum-precipitated toxoid, and the sensitivity of vegetative *Cl. tetani* to antibiotics, the customary indiscriminate prophylactic use of tetanus antitoxin or tetanus toxoid in the early treatment of wounds cannot be justified and should be replaced by more rational treatment. The following scheme is suggested:—

After wounding, actively immunized patients receive 0·5 ml. of fluid toxoid (unless a reinforcing dose has been given during the previous year) and the wound is cleaned surgically. Antibiotics (a single intramuscular injection of 1,200,000 units of benzathine penicillin, or 5 mgm. per kgm. body weight of a "broad-spectrum" antibiotic daily for 3 weeks) are also given if the wound is more severe, or is not treated until 48 hours after wounding, or the patient has not had a reinforcing dose of toxoid during the past 5 years.

In unimmunized patients, superficial wounds are cleaned surgically. An antibiotic (in the above doses) is given if the wound is more extensive, and if the wound is severe, or is not treated until 48 hours after wounding, 5,000–10,000 units of antitoxin are also given.

All unimmunized patients should be actively immunized as soon as possible; the physician giving antitoxin should ensure that active immunization is completed.

A. C. Scott

KATITCH, R. V. Valeur de l'immunité antitétanique après injection de rappel, chez les vaccinées en cours de gravidité. [**Antitetanic Immunity following the Booster Dose after Vaccination during Pregnancy**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 521–4.

Observations were made on pregnant women and confirmed by further observations on pregnant mares. These observations showed that two injections of toxoid at intervals of 3 weeks, given in the later stages of pregnancy, have produced a rise in antibody production much greater than that obtained in normal subjects. A booster dose given 6 months later, however, produced a further rise in antibody content of the sera and did so to an equal extent in those immunized during pregnancy and in the controls. *J. W. McLeod*

BABUDIERI, B. Ricerche serologiche sulla diffusione delle leptospirosi nella provincia di Siviglia. [**Serological Studies on the Diffusion of Leptospiroses in the Province of Seville, Spain**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1960, v. 23, Pt. 6, 515–23.

The English summary appended to the paper is as follows:—

"The agglutination test for leptospiroses has been carried out on 482 human sera collected at random in the province of Seville. Fourteen strains of leptospira belonging to 13 different serotypes were used in performing the reaction. Positive results were given by 97 sera (20·1%) and 58 of these agglutinated at values greater than 1:100. The majority of the positive sera agglutinated *L. ictero-haemorrhagiae,* but reactions were also obtained with *L. pomona, L. bataviae, L. saxkoebing, L. grippo-typhosa* and *L. canicola.*

"The highest percentage of positives was found in sera

from the Guadalquivir delta region where the rice fields are. In this zone only infections with *L. ictero-haemorrhagiae* are observed.

"The cases of infection with *L. pomona* and *L. bataviae* are presumably due to contact with swine carrying these serotypes. In fact 40 out of 41 swine sera tested from the province proved to be positive, often at high titres. Besides antibodies to *L. ictero-haemorrhagiae, L. pomona* and *L. bataviae,* agglutinins were demonstrated for *L. hyos, L. sejroe, L. saxkoebing, L. canicola* and *L. mini.*

"The author draws attention to the importance which the wide diffusion of leptospiroses amongst swine may have both as a source of infection for man, and for the economic loss which they may cause in swine breeding."

MAILLOUX, M. & KOLOCHINE-ERBER, Berthe. Mise au point sur les leptospiroses Outre-Mer (bilan des sérotypes rencontrés). [**Observations on Leptospirosis in Overseas Territories, with a List of Serotypes**] *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 657–66. [67 refs.]

CLARK, L. G., KRESSE, J. I., MARSHAK, R. R. & HOLLISTER, C. J. ***Leptospira pomona* Infection in a Woodchuck. Preliminary Report.** *Pub. Health Rep.* Wash. 1960, Oct., v. 75, No. 10, 925.

MOORE, S. & WHITMORE, D. N. **Case of *Listeria* Meningitis.** [Memoranda.] *Brit. Med. J.* 1960, Nov. 26, 1572–3.

An infant aged 10 days developed typical signs of meningitis and a Gram-positive bacillus was isolated from the cerebrospinal fluid; the bacillus was easily decolorized by acetone so that at first it was thought to be *Haemophilus influenzae,* but was later identified as *Listeria* [*Erysipelothrix*] *monocytogenes.* The organism was sensitive to chloramphenicol and sulphonamides but resistant to penicillin. The child's illness responded rapidly to the first two drugs. A description of the cultural characteristics of the organism is given in some detail. *A. B. Christie*

VIRUS INFECTIONS

The order in this section is:—*General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.*

BAJPAI, P. C., DIKSHIT, S. K., SHARMA, J. C., GUPTA, N. P. & GOVIL, K. K. **Acute Epidemic Encephalitis in Children (Lucknow, 1958). A Clinical Study.** *J. Indian Med. Ass.* 1960, July 1, v. 35, No. 1, 1–13, 2 figs. [20 refs.]

This is a detailed description of the chemical findings in an explosive epidemic of encephalitis occurring mainly among children in Lucknow during July–September 1958 [this *Bulletin,* 1960, v. 35, 486]. It was similar to many other epidemics of encephalitis that have been observed in Northern India since 1954 [*ibid.,* 1956, v. 31, 117; 1957, v. 32, 124]. 301 affected children were admitted to hospital, the majority in the first 4 weeks of the outbreak. Of these, 71 were of fulminating fatal type, and 102 had an acute course, with complete recovery in 98 and neurological sequelae in 4; 15 had a subacute or chronic course, most of them showing evidence of mid-brain damage; and 53 cases ran a relapsing course with ultimate recovery in all but 2. The case fatality rate (children only) was 23·5%.

The neurological signs were very varied, mostly pointing to lesions about the basal ganglia. Meningical signs were frequently but not invariably present, but the spinal fluid findings were near normal, except for increased pressure; there was a tendency to high sugar values in the spinal fluid, and also hyperglycaemia—a feature noted also in some of the other Indian epidemics.

This illness was almost certainly due to a virus infection, but no definite virus was identified. *H. Stanley Banks*

RAMACHANDRA RAO, A., PRAHLAD, I. & SWAMINATHAN, M. **A Study of 1,000 Cases of Smallpox.** *J. Indian Med. Ass.* 1960, Oct. 1, v. 35, No. 7, 296–307, 3 figs.

For 50 years, certainly, the city of Madras has never been free from smallpox, and epidemic levels have been reached every 4–6 years thoughout this period. Usually the highest seasonal incidence has occurred during the months of February to April, and meteorological conditions, especially absolute humidity and the intensity of ultra-violet rays in the atmosphere, have been regarded as determining factors. Yet, for some so far unexplained reason in 1959, a year which followed one of exceptionally high incidence of the disease, the months of August and September showed the highest number of cases. Those here studied were seen in the Infectious Diseases Hospital, Madras, between May and October 1959.

It is well recognized that the most important factor which influences the incidence and the severity of the disease is the vaccination status of the individuals at risk. In the slum areas many children "at the time of vaccination" are "non-traceable", and, furthermore, these areas attract immigrants who are almost invariably unsettled and have not been vaccinated.

In the series of cases under review a distinction is made between the vaccinated—those who bore a scar of successful vaccination—and the unvaccinated—those who showed no evidence of successful vaccination before the commencement of the incubation period of an attack of smallpox.

13 cases of true haemorrhagic smallpox all ended fatally: 8 were in unvaccinated patients aged between 6 and 40 years; 5 occurred in vaccinated subjects of which 4 were in the age-group 21–50. Haemorrhages later in the course of the disease ("variola pustulosa haemorrhagica") were seen in 10 unvaccinated and 5 vaccinated subjects. 11 of these cases were in adults. 3 of the vaccinated and 9 of the unvaccinated patients died.

Of the remaining cases ("confluent", "discrete", and "modified") 430 occurred in unvaccinated and 542 in vaccinated subjects (in the general population the number

of vaccinated exceeds that of the unvaccinated subjects). 60% of the unvaccinated cases occurred in children aged 5 years and under, as compared with 2·2% of the vaccinated. Nearly 65% of unvaccinated patients aged 10 years and below were classified as confluent cases as compared with 12·5% of the vaccinated in the same age-group. A significant difference in type of attack and fatality rate appeared between patients bearing 1 or 2 and those with 3 or 4 vaccination scars.

In view of talk of so-called "placental immunity", it is worth noting that, in this series, nearly 13% of cases in the unvaccinated occurred in infants aged 1 to 6 months.

[Though nothing new emerges from this work, the information derived from this first-hand study of the clinical features of a substantial number of cases of variola major from among a partially protected population, here set out in sensible and lucid detail, is of considerable value. This is a useful paper worthy of closer study.]

J. Pickford Marsden

BEUNDERS, B. J. W., DRIESSEN, J. H. & VAN DEN HOEK, C. **Clinical Picture and Serological Response to Vaccination with Formalinized Vaccinia Virus followed by Scarification with Active Vaccine, in Military Personnel.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 382–94, 5 figs.

For many years—since the early 1920's—the occurrence of post-vaccinial encephalitis has been a matter of concern in the Netherlands. When, in 1945, re-building of the Armed Forces commenced some 120,000 primary vaccinations were performed in the Army and among these 38 cases of encephalitis occurred—5 of which proved fatal.

Some authorities have believed that the encephalitis is a direct effect of the vaccinia virus and have urged simultaneous active and passive immunization with vaccinia virus and anti-vaccinial gamma globulin as a prophylactic measure. Others have held the hypothesis of a commonly circulating virus, usually non-pathogenic but activated by the virus of vaccinia [in other quarters both these theories have been discarded in favour of one of "allergy" or "sensitization"].

This paper gives preliminary announcement of certain work which is being undertaken in an attempt to define a procedure which will reduce the risk of post-vaccinial encephalitis. For serological, and other technical details, of this work the original paper should be consulted.

Of 106,000 soldiers who were primarily vaccinated half received "2 ml. of a 16% immune gamma-globulin", immediately after vaccination. The remainder were given a placebo. 2 cases of encephalitis occurred in the first group, and 10 in the second. It is well recognized that the incidence of encephalitis is markedly lower after revaccinations than after the primary inoculation. In an attempt to achieve "a revaccination status" an experiment has been started whereby people are protected with formalinized vaccine virus before being challenged with live vaccinia virus a few weeks later. Results so far suggest that, although the antigenic potency of the vaccine so far used has been found to diminish rapidly, a satisfactory reduction in the severity of the primary reaction can be obtained by this method; but the question whether thereby the incidence or severity of encephalitis or both can be favourably affected can only be determined after many thousands of vaccinations by this method have been carried out.

J. Pickford Marsden

CUTCHINS, E., WARREN, J. & JONES, W. P. **The Antibody Response to Smallpox Vaccination as measured by a Tissue Culture Plaque Method.** *J. Immunology.* 1960, Sept., v. 85, No. 3, 275–83, 1 fig. [16 refs.]

The authors describe a method of titrating vaccinia virus neutralizing antibody by plaque inhibition in monkey kidney cell monolayers. The method is more precise than most of those at present in use [it compares well with titration by inhibition of pock formation on the chick embryo chorio-allantoic membrane (BOULTER, this *Bulletin*, 1958, v. 33, 404)]. The results are given of a number of titrations of neutralizing and haemagglutination-inhibiting antibodies from subjects of varying vaccination history. Only in primary vaccinations was there any correspondence between the titres of the two sorts of antibody. After revaccinations only neutralizing antibody increased significantly and the titre attained was apparently related to the level of circulating antibody at the time of revaccination.

Colin Kaplan

BAKOS, K. & DINTER, Z. Antikörperreaktion des Rindes auf die Infektion mit dem Virus der Parainfluenza 3. [**Antibody Production in Cattle infected with Parainfluenza 3 Virus**] *Zent. f. Bakt.* I Abt. Orig. 1960, v. 180, No. 1, 1–11, 2 figs. [18 refs.]

The authors have previously isolated para-influenza 3 virus from cattle suffering from a respiratory infection in Northern Sweden [this *Bulletin*, 1960, v. 35, 711], and in the present work the immune response of cattle to infection with the isolated strain has been studied. 2 calves infected intranasally and intratracheally developed inhibiting and neutralizing antibodies in high titres after 7 days, and a similar response was observed in an uninfected calf left in contact. The animals developed a febrile illness with conjunctivitis, rhinitis and salivation. In an investigation of the incidence of inhibiting antibody in the sera of 244 cattle from 41 herds in all parts of Sweden in which a respiratory infection had been observed only 44 (18%) had titres of 8 or less. Antibody was found in 4 persons on a farm in which para-influenza 3 infection was present among the cattle.

D. J. Bauer

DUXBURY, A. E., MCCUTCHAN, R., WHITE, J. & O'KEEFE, L. **Epidemic Adenovirus Infection in a Victorian Migrant Centre presenting as Pharyngo-Conjunctival Fever.** *Med. J. Australia.* 1960, Sept. 10, v. 2, No. 11, 413–17, 2 figs. [11 refs.]

An epidemic of 44 cases of pharyngo-conjunctivitis occurred in a migrant reception centre in Victoria, mainly in children under 4 years of age, between December 1, 1958 and January 17, 1959. There were 600 children at

risk. The disease was characterized by fever, conjunctivitis and pharyngitis of the type described by other workers [*e.g.* BELL *et al.* this *Bulletin*, 1955, v. 30, 824]. There were a number of complications, including 1 case of severe pneumonia, 7 of otitis media, and 2 relapses of the original illness. 10 cases were studied by virus isolation and serum antibody tests. Type VII adenovirus was isolated from all but one, and there was a rise in specific neutralizing antibody in every case. Adenovirus type VII was isolated from 8 of 15 other cases and type III from 1. It was concluded that the epidemic was due to adenovirus type VII. *D. A. J. Tyrrell*

TAI, F. H., GRAYSTON, J. T., JOHNSTON, P. B. & WOOLRIDGE, R. L. **Adenovirus Infections in Chinese Army Recruits on Taiwan.** *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 160–64. [15 refs.]

From December 1958 to the end of March 1959 throat swabs, and eye swabs in a few cases, were collected from 420 Chinese army recruits with acute respiratory disease. 21 adenoviruses were isolated in HeLa cells comprising 7 type 5, 6 type 4, 4 type 3, 2 type 7 and 2 type 8. They were isolated from the throat except for one type 3 which was isolated from an eye swab. Irrespective of the adenovirus type, sore throat, cough and fever were the main symptoms and lasted about 4 days. Only one of the patients from whom type 8 adenovirus was isolated had conjunctivitis.

Paired sera were obtained from 11 of the recruits from whom virus had been isolated. Each pair showed a 4–fold or greater rise in neutralizing antibody titre against the homologous virus and 10 pairs showed a similar rise in complement-fixing (CF) titre against a polyvalent antigen consisting of types 3, 4, 5, 7 and 8. Also, all the pairs tested showed at least one 4–fold heterotypic neutralizing antibody response, most frequently against antibody types 3 and 5. 415 paired specimens of serum from recruits, most of whom were not ill, were taken at the start of training and 12 weeks later; only 25 pairs showed a 4–fold or greater CF antibody rise (6%) and 9 of these rises occurred despite initial CF antibody. The failure of a large epidemic to occur notwithstanding crowding, susceptibility of subjects and the presence of viruses may have been due to the very mild climate (January 52°–64°F.; February and March 59°–72°F.).

D. Taylor-Robinson

HITCHCOCK, Griselda, TYRRELL, D. A. J. & BYNOE, M. L. **Vaccination of Man with Attenuated Live Adenovirus.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 277–82. [15 refs.]

Respiratory infections caused by adenovirus types 3, 4 and 7 occur in epidemic fashion and can be controlled adequately in semi-closed (*e.g.* military) populations by killed polyvalent vaccines [see, for example, this *Bulletin*, 1959, v. 34, 831 *bis*, 832].

The present paper reports the use of living virus for vaccination with adenovirus strains which had been passaged repeatedly in non-primate tissue cultures, such as pig kidney, in an attempt to reduce virulence.

The modified virus was administered intranasally to adult volunteers under conditions of strict isolation. 13 persons were inoculated with type 7 adenovirus; doses as low as 150 TCD50 resulted in significant rises in neutralizing and haemagglutination-inhibiting antibody in those subjects with pre-infective titres below 1 in 16; there was no accompanying rise in complement-fixing antibody; in some there was a heterologous serological response to adenovirus type 3. With higher virus dosage infection occurred despite pre-challenge antibody.

With type 4 adenovirus 2 volunteers given 2,500 TCD50 developed a rise in homotypic antibody without virus recovery or definite illness. 3 volunteers given 250 TCD50 developed neither illness nor antibody rise.

In both these groups the level of virus excretion was low, the virus remained adapted for pig kidney tissue culture and attempted passage to further human volunteers was only sporadically successful; *i.e.* there was no evidence that these live vaccine strains were capable of disattenuation or giving rise to human epidemics. However, it remains to be shown whether this method of vaccination has any advantages in the field over the safer vaccination procedures with killed virus already tested in many centres. *Derek Hobson*

EVANS, A. S., with the technical assistance of Katherine SCHAEFGEN & G. JAKAB. **Infections with Hemadsorption Virus in University of Wisconsin Students.** *New England J. of Med.* 1960, Aug. 4, v. 263, No. 5, 233–7, 1 fig.

This paper reports a further study of respiratory disease in University students [this *Bulletin*, 1957, v. 32, 643; 1959, v. 35, 20]. From January 1957 to April 1959, 175 paired sera from students admitted to hospital were tested by complement fixation (CF) against both Type 1 and Type 2 haemadsorption viruses, 25 paired sera against Type 1 only and 27 against Type 2 only. There was a 4–fold rise in titre against Type 1 in 8·5% and against Type 2 in 1·5%. Isolation studies were hampered by the presence of a simian haemadsorption virus in 20% of the monkey kidney cultures that were maintained in a balanced salt solution containing 2% calf serum. The most common symptoms in 19 patients showing antibody rise were sore throat and fever (over 101°F. in 12 patients), often with cervical lymphadenopathy and cough, both productive and non-productive; these symptoms alone were not characteristic or frequent enough to permit diagnosis. 2 of the cases were considered on clinical and serological grounds to be infectious mononucleosis.

Respiratory disease due to haemadsorption viruses occurred throughout the year with a 4 : 1 male predominance. Widespread infection by Type 1 or an antigenically related virus was suggested by a CF titre above 1 in 8 in almost 75% of the sera tested; only 13% of the sera tested had titres above 1 in 8 against Type 2 virus.

[A control group of healthy students was not studied and virus isolations were not made; it is therefore possible that the antibody rises were due to silent haemadsorption virus infections in patients whose respiratory illnesses were due to some other cause or to infection with a related virus. Further, the clinical picture was unlike that in adults experimentally infected with haemadsorption

viruses who experience mainly symptoms of a common cold. (Reichelderfer, *ibid.*, 1959, v. 35, 176; Tyrrell, *et al. ibid.*, 1960, v. 35, 161).] *D. Taylor-Robinson*

Rowe, D. S. & Michaels, R. H. **Isolation of the Respiratory Syncytial Virus from a Patient with Pneumonia.** *Pediatrics.* Springfield, Ill. 1960, Oct., v. 26, No. 4, 623–9, 2 figs.

An infant, aged 6 months, was admitted to hospital with pneumonia, and discharged after 10 days' treatment with antibiotics and supportive measures. After 24 hours at home she was readmitted suffering from a more severe attack of pneumonia from which she slowly recovered. On this occassion a throat swab was taken and a virus was isolated in tissue culture. The virus behaved in tissue cultures like the respiratory syncytial virus (also called CCA [this *Bulletin*, 1958, v. 33, 407]). During the course of her second illness the patient showed a rise in complement-fixing antibody against the prototype (Long) strain of virus and in neutralizing antibody against her own (Machuca) strain. It is concluded that she was infected with a strain of respiratory syncytial virus, possibly acquired during her first stay in hospital. It is not known whether this virus infection caused her second attack of pneumonia.

[See Beem *et al. ibid.*, 1961, v. 36, 162.]

D. A. J. Tyrrell

Wilt, J. C., Parker, W. L., Owens, A. L. & Stackiw, W. **Enterovirus Infections in Manitoba — 1959.** *Canadian Med. Ass. J.* 1960, Oct. 15, v. 83, No. 16, 839–43, 3 figs.

During 1959, 133 enteroviruses were isolated at the Manitoba Virus Laboratory. Type 1 poliomyelitis virus was the only agent isolated from patients with paralysis. 2 type 1 and 1 type 3 poliomyelitis viruses, 13 Coxsackie B5, 34 ECHO 6, 1 ECHO 9, 2 ECHO 11 and 4 ECHO 20 viruses were isolated from cases of aseptic meningitis. The 4 patients from whose stools ECHO 20 was isolated are described in detail as these are the first reported cases of aseptic meningitis associated with this ECHO serotype. 17 out of 18 patients with epidemic myalgia, who were excreting a virus, yielded Coxsackie B5 (the remaining patient yielded a Coxsackie A virus). Lesser numbers of viruses were isolated from other patients with clinical syndromes. 5 patients had a rash and these were excreting the following viruses: Coxsackie (unspecified), 1; ECHO 6, 1; and poliomyelitis, 3. 28 patients yielded a poliomyelitis virus, 21 being paralytic cases. 5 of these had had a complete course of immunization showing that protection is not absolute. In all, there were 7 cases of poliomyelitis in completely immunized people; 2 were non-paralytic and 3 had residual paralysis. There were 17 cases in non-immunized people of which 2 were non-paralytic, 2 were fatal and 9 had residual paralysis.

A. J. Beale

Van Loghem, J. J. Tropische poliomyelitiscijfers. [**Tropical Polio Statistics**] *Nederl. Tijdschr. v. Geneesk.* 1960, Nov. 12, v. 104, No. 46, 2293–9, 2 figs. [10 refs.] English summary.

In this article Professor Van Loghem continues his studies on the seasonal incidence of poliomyelitis, to assess whether or not seasonal fluctuation is of significance in the epidemiology [see this *Bulletin*, 1955, v. 30, 573; 1957, v. 32, 233; 1959, v. 34, 1230].

As his previous work was on countries not in the tropics, he felt that countries situated about the equator, where seasons are less well defined and day and night nearly of equal length, might clarify a few of the problems, and especially if climate was a factor in the symbiotic relationship of man and virus.

His earlier work (1955 onwards) covering 22 non-tropical countries, amply demonstrated seasonal variation in incidence. Admitting the doubtful value of some of the figures available in the tropics, he felt that the WHO incidence figures (1953–1959) were still worth analysing. The countries selected were: in Africa—Belgian Congo, Kenya, Uganda, Tanganyika; in America—Cuba, Ecuador, Colombia, Venezuela; and in Asia—Ceylon, Philippines, Federation of Malaya, Indonesia, and also Singapore.

Although the evidence was not clear-cut, yet there was no real suggestion of a seasonal variation in the incidence of poliomyelitis (although Kenya and especially Ceylon did not conform) in these tropical countries.

He suggests that these findings further support the claim that the relationship between the poliomyelitis virus and man is influenced by the same climatic factor, the periodicity of which is lost in the tropics.

Kurt Schwarz

Van Tongeren, H. A. E., Wilterdink, J. B. & Timmers, W. C. **Neutralizing Antibodies to the Viruses of Poliomyelitis, Dengue Types 1 and 2, Murray Valley and Japanese B Encephalitis in Papuan Populations of Netherlands New Guinea.** *Trop. & Geograph. Med.* Amsterdam. 1960, Sept., v. 12, No. 3, 208–16, 1 fig. & 1 map. [10 refs.]

Sera were collected from Papuans living around Sentani Lake and Hollandia: the former is separated by high mountains from the Pacific Ocean while the latter is close to it. 347 sera were tested for poliovirus neutralizing antibody in a monkey kidney culture colour test. 54% of children under 5 years of age had antibody to 3 types of poliovirus. In those aged 4–6 years 82, 63 and 66% had antibody to types 1, 2 and 3 respectively. 85% of children under 2 years had type 3 antibody compared with 49 and 30% with types 1 and 2.

Neutralization tests were also made with dengue-1 and dengue-2 in suckling mice with Japanese and Murray Valley encephalitis viruses in adult mice. The sera were screened undiluted and later titrated. No dengue antibody was found in persons under 18 years of age but 20 of 84 persons aged over 20 had antibody. Of 22 sera with dengue antibody, 6 were positive only to dengue-1 and 4 to dengue-2. Only 3 sera had antibody to Murray Valley virus—from persons aged 23, 38 and 42 years. One of

those and no other had antibody to Japanese encephalitis virus. Dengue does not appear to have occurred for over 10 years although *Aedes* mosquitoes are abundant. No wild primates are present in this area.

C. E Gordon Smith

POWELL, B. W. & SMITH, Mary N. **Treatment of Respiratory Paralysis in Small Children.** *Lancet.* 1960, Dec. 3, 1241–3.

This article describes the routine necessary in treating children with respiratory paralysis in Both respirators. The authors found clinical observation more useful than biochemical investigations and were doubtful of the usefulness of abdominal binders at any stage of the treatment. [There is nothing in this article which would not be familiar to workers in respiratory centres.]

A. B. Christie

WORLD HEALTH ORGANISATION. TECHNICAL REPORT SER. No. 203. **Expert Committee on Poliomyelitis. Third Report. Washington, 13–16 June 1960.** 53 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

The WHO Expert Committee on Poliomyelitis met in Washington from June 13 to 16, 1960. They have now issued their 3rd report which is a most interesting and authoritative statement on poliomyelitis [for 2nd Report see this *Bulletin*, 1958, v. 33, 1111]. They review experience with inactivated vaccines and note that the main technical difficulties of manufacture of safe vaccine have now been overcome and that there is a trend towards more potent vaccine. The effectiveness of the vaccine has, in general, reached the level predicted from the original controlled field trial. Less happy experiences have occurred in Hungary and Israel. Major interest in the report will centre on the Committee's recommendations with regard to living vaccine. They make a plea for more research, in particular into genetic stability, the relation of monkey neurovirulence to *in vitro* genetic markers, the importance of simian viruses and the theoretical and practical implications of an attempt to eradicate completely paralytogenic strains of poliomyelitis virus. They believe that the best attenuated strains at present available are Sabin's types 1 and 2, but they do not express a preference among the candidate type 3 strains (Leon 12 ab or Fox) which are less satisfactory.

The need for more research and more experience in the production and use of attenuated poliomyelitis virus is felt to preclude a definite decision about the best method of preventing poliomyelitis. Interim recommendations are:

(1) In a country where poliomyelitis is a disease of infancy or childhood, attenuated vaccine can be recommended.

(2) In communities with many non-immune adults (as judged by more than 20% of paralytic cases occurring in people over 15), it is felt that attenuated vaccine should be used with caution; the safest policy for such a community is to use killed vaccine. If epidemics occur, even in such a community, living vaccine is recommended.

(3) Investigation of the possibility of using living vaccine as a booster dose for infants primarily vaccinated with killed poliomyelitis virus. If the community contains non-immune adults these should have killed vaccine.

(4) If the non-immune adult population is satisfactorily vaccinated, a continuing programme of attenuated poliomyelitis vaccine administration, as under item 1, can be recommended.

(5) Continued surveillance is recommended to establish that safety and potency is maintained (safety particularly for specially vulnerable groups).

The suggestion is also made that a WHO study group should produce recommended requirements for living poliomyelitis vaccine, as has already been done for the killed.

A plea for more exact reporting and investigation of cases of poliomyelitis is again made. Paralytic and non-paralytic (or aseptic meningitis) cases must be reported separately. The pathogenic propensities of the Coxsackie A and B and ECHO viruses is given.

[A short review cannot do justice to this valuable report which constitutes required reading for anyone interested in poliomyelitis. The Committee are to be congratulated on producing a sensible and balanced report on a topic where such sharp differences of opinion exist.

Unfortunately, in their report, statements are made authoritatively without references to the published work that gives support to their statements. It is suspected that sometimes the information available to the Committee has not been published elsewhere.] *A. J. Beale*

PAN AMERICAN HEALTH ORGANIZATION & WORLD HEALTH ORGANIZATION, with the co-operation of SISTER ELIZABETH KENNY FOUNDATION. **First International Conference on Live Poliovirus Vaccines** (Washington, D.C., 22–26 June 1959). Papers presented and discussions held. pp. xiv + 713, illustrated. [Numerous refs.] Scientific Publication No. 44. 1959, Wash. 6: Pan American Sanitary Bureau, Regional Office of the W.H.O., 1501, New Hampshire Avenue, N.W., D.C., U.S.A.

The report of the First International Conference on Live Poliovirus Vaccines has been published with commendable speed but such is the pressure in this field of enquiry that now most of the material has been published elsewhere. Moreover, the 2nd International Conference has now been held and the living vaccines containing Sabin's strains have been approved officially for use in the United States besides being used on many tens of millions in the U.S.S.R.

This first conference was called because many governments were asking the WHO for advice on the status of attenuated poliovaccines. The conference served to underline both the promise and the difficulties of the living poliovaccines. An alternative, cheaper, more effective method of specific immunization against poliomyelitis is clearly desirable. The problems associated with living poliovaccine appear to be immense. Evidence is presented showing variations in monkey virulence (Sabin's strains seem least virulent but MURRAY and MELNICK make all the strains more virulent than their sponsors) and the propensity to increase occasionally in virulence during spread through the community. The antibody response

has varied, depending upon many factors, the response being better in the young, those without antibody, when other enterovirus excretion is rare, when the viruses are given singly and in large doses up to 10^7 TCD50 per ml. Many trials have been initiated throughout the world, although rather few up to the present have been organized by scientists independent of the three originators of attenuated virus strains. These trials have varied in thoroughness of follow-up but none have shown any untoward effects. At present none have shown that the vaccine is effective in preventing poliomyelitis. There can, however, be little doubt that the vaccine will prove effective in those in whom virus multiplies and produces an antibody response.

[This is much too long and detailed a report to abstract fully. It is a mine of information about living polio-vaccine both factual and theoretical.] *A. J. Beale*

TURNER, R. **Live Attenuated Poliovaccine. A Review.** *South African Med. J.* 1960, Nov. 12, v. 34, No. 46, 961–6. [20 refs.]

KOPROWSKI, H. **Tin Anniversary of the Development of Live Virus Vaccine.** *J. Amer. Med. Ass.* 1960, Oct. 22, v. 174, No. 8, 972–6. [13 refs.]

Dr. Koprowski has again presented an amusing and instructive account of the development of attenuated poliomyelitis vaccine from the beginnings in 1950 when he infected a few susceptible subjects with the TN type 2 strain till 1960 when, at the meetings in Washington, over 60 million people were reported to have had attenuated poliomyelitis vaccine. Originally chance mutations had to be selected whereas now the possibility of increasing mutation rates by changing the composition of the nucleic acid with nitrous acid has been demonstrated. The author is convinced of the safety and efficacy of attenuated poliomyelitis vaccine and looks forward to many more anniversary celebrations.

There are some problems still outstanding. Newborn infants respond poorly [PAGANO *et al.* this *Bulletin*, 1961, v. 36, 61]. Interference occurs if all 3 strains are given together or if other enteroviruses are prevalent. Stability of strains in any absolute sense is plainly an impossibility with a replicating agent susceptible to mutation. This admitted, Koprowski denies the importance of such changes for the properties of greatest interest—safety and efficacy.

The presence of extraneous viruses in the attenuated poliomyelitis vaccine is a serious problem although Koprowski believes it has been overemphasized. It is thought that the problem might be overcome by (a) removal of simian viruses by differential adsorption onto ion exchange columns, (b) use of stable early passage human cell lines or (c) the use of infectious RNA in non-primate cells which are not susceptible to the intact poliomyelitis virus. *A. J. Beale*

GEFFEN, T. J. **Poliomyelitis in Vaccinated Subjects, England and Wales, 1959.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Nov., v. 19, 196–8.

GEFFEN and SPICER [this *Bulletin*, 1960, v. 35, 1126] have previously reported the cases of poliomyelitis occurring in persons vaccinated against poliomyelitis in 1958 with an assessment of the efficacy of the vaccine. Now, provisionally, figures for 1959 are presented. There were 1028 notified cases of poliomyelitis of which 739 were paralytic. 33 paralysed patients had had 1 dose of vaccine, 75 2 doses and 40 3 doses. 12 paralysed patients had disease involving the inoculated limb within 27 days of vaccination and another 22 patients were also paralysed within 27 days of vaccination but without involvement of the inoculated limb. The effectiveness of poliomyelitis vaccine was estimated for children under 15 years by calculating attack rates assuming the vaccination status to be that of the population when 50% of the notifications had been made. On this basis the rates per 100,000 for vaccinated and non-vaccinated individuals respectively were as follows: all cases (paralytic and non-paralytic), 2·7 and 16·9; paralytic only, 1·8 and 12·2; and, excluding those with 1 dose from the vaccinated group, 1·4 and 12·4 for paralysed patients. The ratio of paralytic to non-paralytic patients was reduced with increasing numbers of doses being: no vaccine, 2·9; 1 dose, 3·0; 2 doses, 1·9; 3 doses, 1·25. *A. J. Beale*

SPEERS, J. F., CHIN, T. D. Y., MARINE, W. M., HALL, E. C. & GRAVELLE, C. R. **Epidemic Poliomyelitis, Des Moines, Iowa. 1959. Preliminary Report.** *J. Amer. Med. Ass.* 1960, Oct. 15, v. 174, No. 7, 864–8, 3 figs.

There was a severe epidemic of poliomyelitis in Des Moines, Iowa, in 1959 which followed a similar pattern to the epidemics in Chicago in 1956 [NATHANSON *et al.*, this *Bulletin*, 1960, v. 35, 1016] and Detroit in 1958 [BROWN *et al., ibid.*, 1960, v. 35, 677]. These major epidemics have all occurred since the widespread use of Salk poliomyelitis vaccine, although it is as yet uncertain that this is the only factor concerned in the differences between these epidemics and earlier ones. There were 134 cases within the city limits, 53 of which were paralytic. Type 1 poliomyelitis was mainly responsible for the paralytic cases. Evidence for ECHO, Coxsackie and type 3 poliomyelitis virus infection, as well as for poliomyelitis virus type 1 infection, was found among non-paralytic cases. The rates for paralytic poliomyelitis were 3·1 per 100,000 for upper, 29·2 for middle and 58·0 for lower socio-economic groups. The highest incidence was at age 0–4 years but in the 1952 and 1954 epidemics it had been at 5–9 years. The rate for paralytic cases was 20·2 for whites and 136 for Negroes. These epidemiological features were not seen prior to 1956.

In the age-group 0–14 the incidence of paralytic poliomyelitis was 216 per 100,000 for unvaccinated individuals and 20·0 for those who had had 3 doses giving an effectiveness of 90%. Also, the severity of the residual paralysis was less in vaccinated subjects. Thus, 7 out of 17 who had had 3 or more doses made a complete functional recovery whereas only 11 out of 70 patients who had had less than 3 doses did so.

[A more detailed study of the epidemic is promised soon.] *A. J. Beale*

COOK, G. T. & SMITH, A. J. **Serum Neutralizing Antibodies to Coxsackie B Viruses.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Sept., v. 19, 165–9.

4 groups of sera were examined for the presence of antibodies to the first 5 members of the Coxsackie B virus group. Series A sera comprised 100 samples from children sent to the Streptococcal Reference Laboratory of the Public Health Laboratory Service for streptolysin titre. Series B were 100 antenatal sera from Surrey. Series C were 50 sera from venereal disease and maternity clinics in Newport, Monmouthshire and Series D were from 50 blood donors in Leeds. The differences between groups B, C and D were slight. The incidence of antibodies at a dilution of 1/20 for Series A and Series B, C and D, respectively, were as follows: type 1, 11% and 18·5%; type 2, 27% and 59%; type 3, 42% and 28%, type 4, 50% and 62%; type 5, 6% and 14·5%. In general, children had higher titres than adults. This was most noticeable for type 3 and there had been an increased type 3 prevalence just prior to the collection of the sera. The authors conclude that antibodies to the Coxsackie B viruses are probably not uncommon in the general population. [The sera were admittedly not collected in a satisfactory way to give a representative sample of the population.] *A. J. Beale*

DE GÓES, P., DE PAOLA, D., BRUNO-LOBO, M. & DIAS, L. D. Miocardite por vírus Coxsackie do grupo A. [**Myocarditis produced by Coxsackie Virus Group A**] *Anais Microbiol.* Rio de Janeiro. 1959, v. 7, 13–34, 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"Two cases of acute myocarditis in sibling children occurring at the same time are described. One of them died after a short period of illness and at autopsy, lesions suggesting viral myocarditis were observed. In the other case the same diagnosis was established according to the clinical, radiographic and eletrocardiographic data, but the child recovered after four months of illness. In this case a Coxsackie group A type 4 virus was isolated from the stools. This strain when inoculated in baby and adult mice revealed cardiotropism producing focal myocarditis."

TILLEY, J. H. MacD. **Infective Hepatitis in a Mixed School, with High Attack Rate in Females.** *Brit. Med. J.* 1960, Nov. 5, 1354–6, 1 graph.

A small epidemic of infective hepatitis from January to June 1959 was centred on a mixed non-residential school in an urban district, where 27 of the cases occurred. There was no excess of girls over boys in the school; yet 23 of the 27 school cases were in girls and only 4 in boys.

There is no evidence that females usually preponderate in the sex incidences of this disease. The apparent explanation for the anomaly in this instance was temporary inadequate toilet accommodation in the school, especially affecting girls. The epidemiological evidence favoured bowel-to-mouth transmission of the infection; although poliomyelitis vaccination was in progress during the perio there was no evidence of syringe-transmitted infection.

H. Stanley Banks

SINGH, H. N. **Neomycin in Infective Hepatitis.** *Indian Practitioner.* 1959, Dec., v. 12, No. 12, 1035–44 4 figs.

This is a description of 30 cases of infectious hepatiti treated with neomycin, glucose, and vitamins. Neomyci acts on the bacterial flora of the intestine and prevents o reduces ammonia formation. On certain experimenta evidence this is supposed to protect the liver cells fro the destructive action of organisms.

The author considers that improvement in the symptom and signs was remarkable. [This is, however, a subjectiv judgment, justification for which is not very obvious fro the data. It is possible that a controlled trial migh demonstrate no beneficial effect from this treatment.]

H. Stanley Banks

TISZAI, A., FAREDIN, I. & ACSAI, P. Über die Wirkung des Ephedrins auf die 17-Ketosteroid-Ausscheidung bei der Hepatitis epidemica [**The Influence of Ephedrine on 17-Ketosteroid Excretion in Epidemic Hepatitis**] *Wien. med. Woch.* 1960, Nov 12, v. 110, No. 45, 924–6, 3 figs. [31 refs.]

In this paper the authors refer to some of the observations on the effects of cortisone and ACTH [corticotrophin] and of ephedrine in epidemic hepatitis, which have led to the assumption that ephedrine has the property o mobilizing ACTH and influences the pituitary-adrena system.

Studies were made on 16 patients suffering from epidemic hepatitis and 8 healthy controls to determine the effect of ephedrine on the urinary excretion of 17-ketosteroids and the eosinophil blood count. The results are described with diagrams.

Ephedrine by mouth (0·10 gm. and succeeding doses of 0·05 gm. every 2 hours) brought about a 50% reduction in the eosinophil count in 4 hours in both patients and controls. The low urinary excretion of 17-ketosteroids of the patients was increased by ephedrine and gradually reached normal values whereas such increase did not appear in the controls. The authors assume that this increase of 17-ketosteroids excretion in hepatitis is not associated with the adrenal effect of ephedrine but may be attributed to an eventual beneficial influence of the drug on the liver function. *M. E. Delafield*

BLANC, G., ASCIONE, L. & MAILLOUX, M. Les petits mammifères sauvages peuvent-ils être porteurs du virus de la chorioméningite lymphocytaire? Enquête faite au Maroc. [**Can Small Wild Mammals Harbour Lymphocytic Choriomeningitis Virus? Investigations in Morocco**] *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 27/28, 645–9, 5 figs.

During the examination of several species of small mammals wild-caught in Morocco for leptospiral and

rickettsial infections, febrile reactions which could not be attributed to either occurred in guineapigs inoculated with organs. Histological changes in the spleens of inoculated guineapigs and their temperature charts are illustrated. The belief that these infections were due to lymphocytic choriomeningitis virus is based on the fact that the material lost no virulence on exposure to distilled water which was found to destroy spirochaetes and rickettsias. [There is, however, no proof—*e.g.* serological —that the infections described were due to lymphocytic choriomeningitis virus.]

[See also this *Bulletin*, 1960, v. 35, 682.]

C. E. Gordon Smith

Spence, L., Downs, W. G. & Boyd, C. **Isolation of St. Louis Encephalitis Virus from the Blood of a Child in Trinidad, W.I.** *West Indian Med. J.* 1959, Sept., v. 8, No. 3, 195–8.

A blood sample was obtained on September 15, 1958 from an 11-year-old boy at Sangre Grande who had had fever for 3 days with headache and cough. The fever continued for 1 week after and recurred on October 2 lasting 2 days with headache, abdominal pain and splenomegaly. Virus was isolated from the first but not the October 3 blood sample by inoculation of 2-day-old mice. It was virulent also for adult mice. The serum virus titre was 1·4 log LD50. Complement-fixation and haemagglutination-inhibition tests showed that the virus isolated was identical with or closely related to St. Louis virus (Tr 9464 strain) and haemagglutination-inhibition and neutralization tests on serial serum specimens from the patient confirmed that the isolated virus had been the cause of his febrile illness.

[See also this *Bulletin*, 1958, v. 33, 413, *bis*.]

C. E. Gordon Smith

Libíková, H., Blaskovic, D., Vilcek, J., Řehácek, J., Gresíková, M., Macicka, O., Ernek, E. & Mayer, V. **Incidence of Antibodies against Tick-Borne Encephalitis Virus in Man and Domestic Animals in a Small Village in a Natural Focus of Infection.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 327–32.

Sera were collected in Nemcinany in the Zlaté Moravce district which is a known focus of tick-borne encephalitis. Sera were tested in a neutralization test in HeLa cells against the Hypr strain after 42 mouse and 24–27 HeLa cell passages. 34 of 191 human sera were positive. The age distribution was: 6–19 years 7%, 20–34 years 22%, 35–49 years 15%, 50–64 years 55%. 5% of 82 schoolchildren, 22% of 32 housewives and 33% of 57 farm workers had antibody. Of 49 goat sera 16 were positive. Of 174 sheep sera from animals in close contact with forest, 41 were positive. In a herd of old cattle 49 of 98 had antibody while in a herd aged under 1 year which had not yet been driven to pasture only 4 of 98 had antibody. Serum titres of 1:8 to 1:2,048 were found but most commonly 1 : 8–1 : 32 in both man and animals. Only 6 of the human beings with antibody had a history of encephalitis. *C. E. Gordon Smith*

Vereta, L. A. & Kanter, V. M. **Study of Tick-Borne Encephalitis of Alimentary Origin in the Khabarovsk Region.** *Problems of Virology.* London. 1960, v. 5, No. 2, 216–20. [Translated from Russian.]

A proportion (16% in 1957) of cases of tick-borne encephalitis in the Khaborovsk region have no history of tick-bite and family outbreaks suggestive of milk-borne infection occur. 5 such outbreaks were studied in which there were 13 cases, 10 of the patients being children or adolescents. The disease was severe with residua in 2 and death in 5. Antibody was found in 6 other members of these families [paired sera were not examined]. The goats belonging to the families had high antibody titres as did the cows of one family (one cow showed a rise in neutralizing index from 251 in July to 2,818,000 in August). The history of these outbreaks and the presence of infection in the milk animals suggests, but does not prove, that milk-borne infections as well as tick-borne infections occur in the Khabarovsk region. If these are milk-borne infections then their severity is marked compared with the mild type of disease which follows milk transmission in western U.S.S.R. *C. E. Gordon Smith*

Tiushniakova, M. K., Zagromova, M. S. & Federov, I. V. **Production of a Diagnostic Antigen for the Complement-Fixation Test in Tick-Borne Encephalitis.** *Problems of Virology.* London. 1960, v. 5, No. 2, 221–5. [16 refs.] [Translated from Russian.]

The Kargasoksii strain of tick-borne encephalitis virus isolated from *Ixodes persulcatus* was used. A 10% suspension of infected mouse-brain titring 8–10 log LD50 was kept at 4°C. for 24 hours then centrifuged. It was then frozen and thawed 5 times and again centrifuged. 45 ml. of methyl alcohol at −20°C. was then added to each 100 ml. and the mixture held at 4°C. for 18–24 hours, then centrifuged. The sediment was dissolved in buffered saline and had an infectivity of 7–8 log LD50. 40% formalin was then added to a concentration of 1 : 1000 and the mixture was held at room temperature for 6 days. It was non-infective at this stage. 20% sucrose and 2% gelatin were then added and the antigen lyophilized. The antigen was stored without loss for 1 year at 4°C. Sera from patients with tick-borne encephalitis were tested in complement-fixation (CF) tests with this antigen: 62% of sera collected 1–3 days after onset had CF antibody, 64% of those 4–6 days from onset, 66% 7–10 days after onset, 74% 11–15 days after onset, 80% 16–30 days after onset, and 50% 30–42 days after onset. [These very high figures early in the course of the disease are surprising.] Early sera gave titres of 4–8, between the 4th and 10th days 4–16, 11–30 days 16–64 and later 16–128. Sera from patients with other diseases gave negative results. *C. E. Gordon Smith*

McLean, D. M., MacPherson, L. W., Walker, Selma J. & Funk, Gloria. **Powassan Virus: Surveys of Human and Animal Sera.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1539–44. [15 refs.]

Unheated sera were tested for neutralizing antibody to Powassan virus [this *Bulletin*, 1960, v. 35, 717] in an

intracerebral test in mice. They were also tested for complement-fixing antibody to Powassan, St. Louis, eastern and western equine encephalitis viruses with borate-saline extracts of mouse brain as antigens. Human sera were collected in 4 places in Northern Ontario: 1 of 6 from Powassan, 2 of 65 from North Bay, 3 of 52 from Manitoulin Island, and none of 57 from Sault Ste. Marie had neutralizing antibody to Powassan virus but none of them had complement-fixing antibody to any of the viruses used. Neutralizing antibody was found in 4 of 13 chipmunks (*Tamias striatus*), 1 of 9 squirrels (*Tamasciurus hudsonicus*) but not in 4 field mice, 2 rabbits, 2 horses, 2 cows, 2 dogs and 14 birds from the Powassan area, nor from a squirrel and 5 birds from Manitoulin Island. 11 birds from the Algonquin Park were also negative.

No ticks were found on animals except *Haemaphysalis leporis-palustris* on the rabbits. 50 ticks were ground up and inoculated into suckling mice as were *Aedes* spp. mosquitoes collected coming to bite man near Powassan, but no virus isolated.

2-day-old chicks inoculated subcutaneously with Powassan virus almost all circulated virus from the 3rd to the 7th day after inoculation and 10 of 14 developed antibody. The highest titres (5 log LD50/0·03 ml.) were on the 3rd and 4th days. Hamsters circulated virus 2, 4 and 5 days after inoculation subcutaneously with 4 log LD50; 3 of 6 given 10 LD50 had viraemia: all developed antibody. Of 2 laboratory rabbits given 4 log LD50 subcutaneously, 1 had a low viraemia and both developed antibody. *Culex fatigans* were inoculated with 3 log LD50 but no virus was detected in them after 4 and 7 days' incubation at 80°F. *C. E. Gordon Smith*

Bárdos, V., Adamcová, J., Balát, F. & Hudec, K. **The Study of Natural Focal Character of the "Tahyna" Virus by Serological Examinations of Birds.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 282–6. [11 refs.]

Sera were collected in April and August 1959 in south-east Slovakia in the region where Tahyna virus was isolated [this *Bulletin*, 1960, v. 35, 207] and also in August in the northern foothills of Slovakia. Some of the blood samples were collected on filter paper discs. The sera were tested for neutralizing antibody by using an intracerebral test in mice and 50–100 LD50 of the "92" strain of virus. In spring, sera were collected from 205 birds of 30 species and 4 were positive and 14 inconclusive; in summer 307 sera from 56 species yielded 34 positive, and 39 inconclusive sera. [Unfortunately from here onward in the paper the inconclusives are treated as positives which may not be justified in a collection of bird sera from many species in which little serology has been done.] More migratory birds (25%) than non-migratory (13%) had antibody—a significant difference (p 0·001). 13% of adult birds had antibody compared with 29% of juveniles. There was no obvious relationship between nesting site and incidence of antibody. 20 of 120 sera from the northern foothills, where the virus was not known to occur, suggest that it has a wider distribution than previously thought. Only 1 of 80 rodent sera diluted 1:2 to 1:3 had antibody [species not stated]. *C. E. Gordon Smith*

Gresser, I. & Katz, S. L. **Isolation of Measles Virus from Urine.** *New England J. of Med.* 1960, Sept. 1, v. 263, No. 9, 452–4. [21 refs.]

Specimens of urine ranging from 2 to 250 cc. were taken from 11 children aged from 2 to 9 years suffering from measles. The *p*H was adjusted to 7·0–7·2 with sodium bicarbonate; penicillin and streptomycin were added, and the urine was centrifuged for 30 minutes in the cold. Aliquots of the supernatant fluid and the sediment were then inoculated into human kidney monolayer cultures. Measles virus was thus isolated from 6 of 8 patients from samples taken 1 day before the appearance of the exanthem up to 4 days afterwards, but could not be found in urine collected from 4 patients 5–12 days after the appearance of the exanthem.

D. J. Bauer

Bhaduri, B. N. **Congenital Ocular Defects in Infants following Measles during Pregnancy.** *Calcutta Med. J.* 1960, Aug., v. 57, No. 8, 269–71.

Since 1955, examination of infants with cataract at the Chatterjee Eye Hospital, Calcutta, has included an enquiry into a history of infections in the mother during pregnancy. In about 2 dozen cases of cataract, a history of measles in the mother during about the 5th to 12th week of pregnancy has been obtained for 5 mothers. The ocular defects observed were microphthalmos (associated with microcephalus) and cataract in one or both eyes; a congenital heart defect was also present in 1 case. One of the 5 patients had no cataract, but a corneal opacity which may have been due to congenital syphilis. In the 4 apparently true instances of congenital defect following maternal infection during pregnancy, the history was medically confirmed only in 2. [There seems to be some evidence here of congenital infantile cataract following measles in the mother at the 5th to 8th week of pregnancy in a small proportion of the persons at risk, but the evidence is poorly documented. This matter is unlikely to be settled without several large *prospective* enquiries.] *H. Stanley Banks*

New England J. of Med. 1960, July 28, v. 263, No. 4, 153–84, 8 figs. [51 refs.] **Studies on an Attenuated Measles-Virus Vaccine.**

In a series of 8 papers devoted to live attenuated measles vaccine the laboratory and preparative aspects are described, and the results obtained in clinical practice by a number of independent groups of investigators are presented.

J. F. Enders, S. L. Katz, M. V. Milovanovic and A. Holloway (*Development and Preparation of the Vaccine: Technics for Assay of Effects of Vaccination*, pp. 153–159) review early work on measles virus, the isolation of the Edmonston strain and its adaptation to chick embryo monolayers and use as a vaccine. Two types of vaccine were used in the present study, both of which consisted of the supernatant fluid of infected cultures, with the addition of 2·5 or 5% (Vaccine A) or 1·1% (Vaccine B) human serum albumin as a stabilizer. The vaccine contained only small amounts of infective virus

(titres 2·5–3·3 log units per ml.); it did not produce disease or consistent viraemia in susceptible cynomolgus monkeys, but nevertheless provoked a good immune response.

S. L. Katz, J. F. Enders and A. Holloway (*Clinical, Virologic and Immunologic Effects of Vaccine in Institutionalized Children,* pp. 159–161) administered 0·2 ml. of vaccine A subcutaneously to 11 of 13 susceptible children, aged from 2½ years to 10½ years, resident in an institution in Boston, and the remaining 2 were observed as controls. No local reactions occurred; 8 vaccinated children developed pyrexia of 100°F. or higher after 6–9 days, which persisted for 2–5 days, and 9 developed a macular rash at the end of the febrile period. There was no catarrh or impairment of well-being. A satisfactory immune response developed in all instances. No signs of infection were detected in the control children.

C. H. Kempe, E. W. Ott, L. St. Vincent and J. C. Maisel (*Clinical and Antigenic Effects of Vaccine in Institutionalized Children,* pp. 162–165) carried out a similar investigation in Colorado; 33 of 69 children aged up to 18 years who were resident in institutions were given 0·1 ml. of vaccine A subcutaneously or intradermally, and 21 showed clinical or serological evidence of infection. In the remaining children a clinical and serological response appeared after subcutaneous vaccination in 4 of 8 given 0·05 ml., none of 7 given 0·2 ml. (who were found to possess measles antibody before vaccination) and in 8 of 13 given 0·5 ml., and after intradermal vaccination in 2 and 4 respectively of 8 given 0·05 ml. No response was obtained in 29 children revaccinated after 21 days, only 5 of whom had responded to the first vaccination; antibody was present initially in 18 who failed to respond to either vaccination. No evidence of spread of infection was obtained in 12 susceptible children in contact. The disease which appeared as a response to vaccination was mild, and conjunctivitis, coryza or cough were not observed.

F. L. Black and S. R. Sheridan (*Administration of Vaccine by Several Routes,* pp. 165–169) administered both types of vaccine to 40 susceptible children aged from 2 weeks to 12 years who were inmates of an institution in Connecticut. A clinical or serological response was obtained in all of 9 children vaccinated subcutaneously, none of 10 given the vaccine by oral swabbing, 1 of 10 given vaccine in the conjunctival sac, and 4 of 11 vaccinated intranasally. No evidence of transfer of infection could be obtained in 10 susceptible children who were in contact.

M. L. Lepow, N. Gray and F. C. Robbins (*Clinical, Antigenic and Prophylactic Effects of Vaccination in Institutionalized and Home-Dwelling Children,* pp. 170–173) administered both types of vaccine subcutaneously to 54 susceptible children, aged up to 10 years, resident in an institution and in private houses in Cleveland, Ohio. 47 gave a clinical response to vaccination, fever being observed in 40, a rash in 23, coryza in 15 and Koplik spots in 10.

S. Krugman, J. P. Giles and A. M. Jacobs (*Clinical, Antigenic and Prophylactic Effects of Vaccine in Institutionalized Children,* pp. 174–177) gave vaccine B subcutaneously to 23 susceptible children resident in an institution in New York. Fever of 1–5 days' duration developed in 90%, and a rash in 11 of 18 children, which appeared after 11–15 days when the fever was subsiding. Coryza, cough and conjunctivitis were not observed. The infection was not transferred to 23 susceptible children who were in close contact. An epidemic of measles occurred in the institution 7 weeks after vaccination; the 23 vaccinated children were unaffected, whereas 17 of the 23 unvaccinated controls developed the disease.

R. J. Haggerty, R. J. Meyer, E. Lenihan and S. L. Katz (*Clinical, Antigenic and Prophylactic Effects of Vaccine in Home-Dwelling Children,* pp. 178–180) administered vaccine A subcutaneously to 39 children living at home in Boston who had no previous history of measles. Fever lasting from 2 hours to 5 days developed after 6–10 days in 35 children, 18 developed a macular rash after 7–13 days, conjunctivitis appeared in 10, cough in 20 and coryza in 19, although the respiratory symptoms could have been due to an intercurrent infection. No case of measles occurred among 16 vaccinated children exposed to infection during the 4 months after vaccination, whereas 7 cases occurred among unvaccinated children in the same families.

In a final paper (*General Summary and Evaluation of the Results of Vaccination,* pp. 180–184), by S. L. Katz, C. H. Kempe, F. L. Black, M. L. Lepow, S. Krugman, R. J. Haggerty and J. F. Enders the results presented in the preceding papers of this series were summarized and discussed. *D. J. Bauer*

Lebedev, D. D., Dadash'ian, M. A., Fadayeva, L. L. & Prokhorovich, Y. V. **Study of the Efficacy of Active Immunization against Measles.** *Problems of Virology.* London. 1960, v. 5, No. 2, 235–40, 2 figs. [Translated from Russian.]

"(1) The measles tissue culture vaccines prepared in the Institute of Virology of the Academy of Medical Sciences of the U.S.S.R. under the direction of V. M. Zhdanov and tested by us produced only slight reactions.

"(2) In view of the small number of children immunized who came into contact with measles, we cannot draw any definite conclusions on the epidemiological efficacy of the 3 vaccines tested. Nevertheless, the clinical observations on 12 children who though immunized against this infection developed measles are highly encouraging (absence of complications in 11 of 12 children with a shortened acute period and a general well-being; in some of the children subfebrile temperatures were present with the absence of the phase character of the eruptions)."

Ström, J. **Infectious Mononucleosis—is the Incidence Increasing?** *Acta Med. Scandinavica.* 1960, Sept. 21, v. 168, No. 1, 35–9, 5 figs. [10 refs.]

The chief physician of the Hospital for Infectious Diseases, Stockholm, has observed a gradual and considerable increase in the cases of infectious mononucleosis admitted to the hospital in the last 20 years. An analysis of 1,779 patients admitted during the years 1940–57 showed a 6-fold rise in the number of cases and a 4·4-fold rise per 100,000 population. It is largely a disease of youth (15–25 years of age) but rather more

than a third of the patients were children. Males preponderated at all ages except in the 15–19-year group.

Social, medical, and diagnostic difficulties may have been responsible for some small part of the increase, but a substantial real increase is probable. The difficulty in exact assessment is the uncertain aetiology—which may well be multiple. That a virus is concerned is suggested by the finding of serous meningitis in 28% and abnormal electro-encephalograms in 38% of 125 cases in Scandinavia [nothing like these percentages have yet been found in the United Kingdom]. In order to extend our knowledge, the disease should be made notifiable.

H. Stanley Banks

Janbon, M., Bertrand, L. & Dorst, V. La rupture de la rate dans la mononucléose infectieuse. [**Rupture of the Spleen in Infectious Mononucleosis**] *Giorn. di Malattie Infettive e Parassit.* 1960, July, v. 12, No. 7, 321–41, 9 figs. [Numerous refs.]

This is a long and detailed account of rupture of the spleen in infectious mononucleosis. The authors have collected particulars of 41 cases including 2 of their own. The underlying condition is friability of the enlarged spleen consequent on mononuclear infiltration and oedema of the capsule and trabeculae, as found by some observers, or a similar infiltration of the intratrabecular vessels, sub-intimal in the veins and sub-adventitial in the arteries, as found by the authors in their two cases and by many others. These vascular lesions produce a separation of the coats of the vessels and lead to haemorrhage. This most usually produces a sub-capsular haematoma, accompanied by abdominal pain in the left hypochondrium and ultimately by grave shock when the haemorrhage invades the peritoneum.

The condition is predominant in males (80%) at ages 19–29 years (82%), and is frequent in young soldiers (41%); a history of trauma was found in only 20% of the cases, and in 80% the rupture appeared to be spontaneous or quasi-spontaneous (several cases occurred during or just after defaecation). Occasionally rupture of the spleen is the first apparent symptom of the disease, but it usually occurs as a complication in the 2nd or 3rd week.

For diagnosis the most important practical point is awareness of this complication of infectious mononucleosis. Whatever the anatomical type of the lesion—capsular laceration, sub-capsular haematoma, or intrasplenic haematoma—the inevitable denouement in all untreated cases is sub-peritoneal haemorrhage. The treatment in all cases, therefore, is surgical—splenectomy as soon as the diagnosis is made. Out of 32 cases in which the operation was performed there were 30 recoveries (2 patients died of late pulmonary embolism), and out of 9 cases without surgical intervention all were fatal.

H. Stanley Banks

Williams, G., Stretton, T. B. & Leonard, J. C. **Cytomegalic Inclusion Disease and *Pneumocystis carinii* Infection in an Adult.** *Lancet.* 1960, Oct. 29, 951–5, 5 figs. [36 refs.]

This is a description of a fatal case of combined cytomegalic inclusion disease and *Pneumocystis carinii* infection in a man aged 25. The patient had severe ulceration of the nose and lip and perianal region associated with very severe constitutional symptoms. Bronchopneumonia and staphylococcal empyema were terminal events. Post-mortem examination showed grey-white consolidation of portions of both lungs and large cells typical of cytomegalic inclusion disease were present throughout. Light-refracting bodies characteristic of the cysts of *Pneumocystis carinii* were scattered throughout the lungs. The oral and perianal ulcers appeared to be non-specific granulomata but intranuclear inclusions were found in some of the cells. Cytomegalic inclusion is found in the adult usually in association with some serious underlying disease such as myeloid leukaemia, but in this case no other disease—apart from the terminal staphylococcal infection—was found.

A. B. Christie

Cullen, S. I. **Cat-Scratch Disease presenting as Bilateral Inguinal Lymphadenitis.** *New England J. of Med.* 1960, Oct. 27, v. 263, No. 17, 851–2.

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

KING, M. K. **Pathogenesis of Fever: Effects of Various Endogenous Pyrogens upon the Level of Circulating Granulocytes in Normal Rabbits.** *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 809–19, 5 figs. [17 refs.]

Another in a long series of papers by King and his colleagues on the pathogenesis of fever, this paper deals with a comparison of the effects upon circulating leucocytes in the normal rabbit of intravenous injections of (a) endogenous pyrogen (serum from rabbits injected with bacterial endotoxin in the form of undiluted typhoid vaccine), (b) the cell-free fluid from a sterile peritoneal exudate, and (c) bacterial endotoxin in the form of diluted typhoid vaccine. The endogenous pyrogen produced a sudden, marked, but brief leucopenia, followed by a considerably leucocytosis; the peritoneal exudate fluid caused a leucocytosis without the preceding leucopenia, while the comparably pyrogenic doses of typhoid vaccine made no significant change in the level of circulating leucocytes. It is suggested that the leucopenia which classically follows the injection of bacterial pyrogens may be caused by the newly-formed endogenous pyrogen rather than by the bacterial pyrogen itself. The brevity of the leucopenia following the injection of endogenous pyrogen suggests that the granulocytes have temporarily become stuck to capillary endothelium or become sequestered in the lungs, liver or spleen. The rapid re-entry of the same cells into the circulation would account for the sudden shift from a marked leucopenia to a leucocytosis in such a short period. *D. A. Cannon*

LANG, K. Experimentelle Studien über die hemmende Wirksamkeit der Anreicherung nach Kauffmann. **[Experimental Studies on the Inhibiting Effect of Enrichment according to Kauffmann]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 2, 221–33.

The English summary appended to the paper is as follows:—

"Comparative experiments were conducted on the inhibiting effect of the brilliant-green-sodiumtetrathionate enrichment made according to different directions for preparation, with the addition of bile according to KAUFFMANN. These experiments demonstrate that only the enrichment made with an iodine-potassium iodide solution, (20 Gr. iodine + 25 Gr. potassium iodide + distilled water to 100 ml.), and not heated, corresponds to the performance demanded from a salmonella selective medium. In the sphere of Gram-negative secondary flora the tetrathionate effect promoted by the addition of beef bile dominates, while in the sphere of the Gram-positive secondary flora the brilliant green effect dominates. This remarkable effect of the brilliant green on the Gram-negative secondary flora in the concentration of 1:100,000 is to a great extent cancelled by the addition of beef bile, and, therefore, is not obvious in the enrichments, as with E. coli, or only very little, as with Proteus. Accordingly, in the enrichment process neither a summation nor a potentiation of the effects of the various effective components is given by the combination, especially in the sphere of the Gram-negative secondary flora; there is even a functional incompatibility between brilliant green and beef bile."

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

KOOPMANS, R. K. **A New, Simple, Quantitative Micromethod for the Rapid Determination of Bacterial Susceptibility.** *Antibiotics & Chemotherapy.* New York. 1960, Oct., v. 10, No. 10, 612–22, 5 figs. [15 refs.]

The method described in this paper from Groningen, Holland, employs a thin layer of a clear solid medium on a slide on which it is surrounded by a rim. This medium is inoculated by streaking with a horse hair ("the only material that never damages the surface") charged either with culture suspension or with an actual specimen from a patient. There are 20 ruled lines on each slide to act as guides for inoculation with 20 different organisms. The preparation is examined microscopically after 4 hours to determine whether the antibiotic concentration in the medium has sufficed to inhibit growth, several slides being used for each test containing different concentrations. Comparative tests made by this and a conventional tube dilution method

showed good concordance. [There is much in the paper about counting numbers of individual bacteria in groups or microcolonies, and their significance, but not enough is said about technical details to enable anyone to try this method: the medium is not specified, nor its depth, nor whether, and if so how, it is covered.]

L. P. Garrod

WATSON, K. C. & JOUBERT, S. M. **Haemagglutination of Cells treated with Antibiotics.** [Correspondence.] *Nature.* 1960, Nov. 5, v. 188, 505–6.

These authors from Durban, who have previously studied the agglutination of penicillin-treated red cells by human sera [this *Bulletin,* 1959, v. 34, 562], have examined 1,700 specimens of serum for capacity to agglutinate red cells treated with other antibiotics. Results with streptomycin and tetracycline were negative, but 6 sera agglutinated cells treated with chloramphenicol, the titre varying from 2 to 128. Whereas 28 of 30 sera agglutinating penicillin-treated red cells were from subjects who had received penicillin treatment, only 1 of 6 positive sera came from subjects with a history of treatment with chloramphenicol. It is not certain whether the substance concerned is " of immune origin ", and its nature is still being investigated. *L. P. Garrod*

GARROD, L. P. **The Relative Antibacterial Activity of Four Penicillins.** *Brit. Med. J.* 1960, Dec. 10, 1695–6.

The penicillins tested were penicillin G, phenoxymethylpenicillin (penicillin V), phenethicillin (alpha-phenoxyethylpenicillin; Broxil), and 6-(2,6-dimethoxybenzamido) penicillanate monohydrate (BRL 1241; Celbenin, methicillin). When their antibacterial activities were compared by a plate dilution method against the commoner pathogenic bacteria, penicillin G was found to be the most powerful followed (in descending order of activity) by penicillin V, Broxil, and Celbenin. Two uncommon species of Proteus were exceptions in being more sensitive to Celbenin and Broxil.

The differences in activity were sometimes wide; a concentration of Celbenin 64 times that of penicillin G was needed to inhibit penicillin-sensitive staphylococci. The minimal inhibitory concentration of penicillin V for *Neisseria gonorrhoeae* was 4 times that of penicillin G, which may explain the ineffectiveness of penicillin V in the treatment of some cases of gonorrhoea.

Penicillinase-forming staphylococci were not included in the bacteria tested. With identical inocula, however, they would be as sensitive to Celbenin as other staphylococci but would show progressively greater resistance to Broxil, penicillin V, and penicillin G in keeping with the different rates of antibiotic inactivation by penicillinase. *J. M. Stark*

CURRENT THERAP. RES. New York. 1960, Oct., v. 2, No. 10, 509–23. **Abstracts of Papers presented at a Conference. A New Synthetic Penicillin: Experiences in the Therapy of " Resistant " Staphylococcal Disease.**

This report comprises abstracts of 18 papers presented at a Conference held at Syracuse, N.Y., on Sept. 7, 1960, on the subject of the new penicillin here described as 2,6-dimethoxyphenyl penicillin, or " penicillin X-1497 " (it is apparently to be marketed in the U.S.A. as Staphcillin: it is what is known in Great Britain as Celbenin or methicillin). The contents of these papers are naturally repetitive, and most of the information they contain only confirms that in a series of papers by which this discovery was announced in England [this *Bulletin,* 1961, v. 36, 150, 173, 174, 175].

Almost all the authors have confirmed that staphylococci, however resistant to other penicillins, are uniformly sensitive to X-1497 in concentrations in the order of 1–6 μgm./ml. There is a little information about action on other species, showing in general that such organisms as streptococci, *Proteus* spp. and various anaerobes are less sensitive to X-1497 than to penicillin G. Several authors have confirmed that staphylococcal penicillinase has no, or almost no, action on X-1497. In one study it was found to exhibit almost no synergy with streptomycin against enterococci or staphylococci, although penicillin G did so.

Clinical studies include numerous rather fragmentary items about blood levels attained at different intervals after doses, but several authors provide the useful information that the maintenance of good blood levels can be prolonged with probenecid. One author tried giving 1 gm. by the mouth, and could detect none at all in the blood. Several series of therapeutic results are reported, although in abstract form they lack enough description to give the reader any real picture of the patients. Most had staphylococcal infections (septicaemia, pneumonia, osteomyelitis, etc.) and the department reporting uniform success in 10 such cases gave doses of up to 15 gm. daily, but there were also some streptococcal infections (including endocarditis) in which success was obtained. All authors are unanimous in their verdict that X-1497 has a low toxicity, but their findings are discordant about the relation between sensitivity to X-1497 (the usual manifestations of which were seen in a few patients) and to penicillin G, some saying that a patient sensitive to G reacted in the same way to X-1497, and others that single patients did not. [Cross-sensitivity has been observed in England. It would certainly be safer to rely on positive findings in this connexion rather than the negative.] *L. P. Garrod*

CRONK, G. A., WHEATLEY, W. B., FELLERS, G. F. & ALBRIGHT, H. **The Relationship of Food Intake to the Absorption of Potassium Alpha-Phenoxyethyl Penicillin and Potassium Phenoxymethyl Penicillin from the Gastrointestinal Tract.** *Amer. J. Med. Sci.* 1960, Aug., v. 240, No. 2, 219–25, 2 figs.

A single tablet of potassium alpha-phenoxyethyl penicillin was given to healthy adults 60, 30 and 15 minutes before and with and 2 hours after a standard lunch. The blood levels attained half and 1 hour after the dose were higher when the dose was taken before food, particularly in those taking it 60 minutes before. At 2 hours there was little difference: no observations were made after this [it would have been interesting to

know whether, in this series of tests, the evidently slower absorption with food prolonged the effective blood level].

A similar experiment was done in which equivalent doses of this penicillin and of phenoxymethyl penicillin were compared: the intervals here were 1 hour before, with and 1, 2 and 3 hours after food. This showed that both penicillins were affected in the same way by the relation of the dose to a meal, absorption being better before it, and that phenoxymethyl penicillin is less completely absorbed, the levels being generally lower.

L. P. Garrod

KUSHNER, D. J. **An Immunological Study of *Bacillus subtilis* Penicillinases.** *J. General Microbiol.* 1960, Oct., v. 23, No. 2, 381–92, 5 figs. [15 refs.]

Penicillinase was extracted from 2 strains of *Bacillus subtilis*. Unlike that of *Bacillus cereus*, the penicillinase of *B. subtilis* is not adsorbed on glass: from 1 strain it was concentrated by calcium phosphate gel adsorption and from the other by simple evaporation. Rabbits were immunized with both preparations and the capacity of their sera to neutralize and precipitate these and other penicillinases was determined. They had no neutralizing action on *B. cereus* penicillinase. They neutralized both basal and induced *B. subtilis* penicillinase equally. Cross-reactions between the 2 sera and the 2 *B. subtilis* penicillinases used to produce them gave peculiar results: one serum was more active in neutralizing the homologous penicillinase, but the other, although much weaker, was more active against the heterologous.

L. P. Garrod

FINLAND, M. & GARROD, L. P. **Demethylchlortetracycline.** *Brit. Med. J.* 1960, Oct. 1, 959–63, 4 figs. [49 refs.]

This article discusses all the published, and some unpublished, information about demethylchlortetracycline (DMCT), one of a new group of tetracyclines which have one methyl group fewer than oxytetracycline (OTC), chlortetracycline (CTC) and tetracycline (TC).

DMCT is highly resistant to acids and alkalis. Although the highest blood level is reached more slowly than with OTC, CTC, and TC after a single oral dose of 500 mgm., renal clearance is low and therapeutic blood levels persist longer than with the other 3 tetracyclines after both oral and intravenous doses. DMCT is on average twice as active as TC against many Gram-positive and Gram-negative pathogens *in vitro*; against resistant staphylococci its relative activity is less marked. Clinical reports indicate that in smaller doses it is as effective as OTC, CTC, and TC, and it has been found as effective as, or more effective than, TC in experimental infections in mice. Because of its greater activity and persistence in the blood the authors suggest that it need be given twice daily only, and that smaller doses should produce an equal therapeutic effect. It is not clear if DMCT causes "tetracycline diarrhoea" more readily than the other three tetracyclines; diarrhoea occurs more frequently if doses over 1 gm. a day are given. A specific phototoxic reaction was observed in patients exposed to sunlight of wavelength 2,700–3,200 Å while taking DMCT: sunlight of this wavelength occurs rarely in Great Britain.

A. C. Scott

SIEGENTHALER, W., BROVELLI, L., STUTZ, R. & WIESMANN, E. Klinische und experimentelle Untersuchungen mit Demethylchlor-Tetrazyklin, einem neuen Breitspektrum-Antibioticum. [**Clinical and Experimental Studies of Demethylchlortetracycline, a New Broad Spectrum Antibiotic**] *Schweiz. med. Woch.* 1960, Nov. 12, v. 90, No. 46, 1315–21, 4 figs. [19 refs.]

This study affords confirmation from Zurich of findings already reported from the United States and elsewhere [see, for example, this *Bulletin*, 1959, v. 34, 1036; 1960, v. 35, 384]. The authors found that demethylchlortetracycline (DMCT) was more active *in vitro* than the other tetracyclines against 10 strains each of *Escherichia coli* and *Staphylococcus aureus*, that the administration of 600 mgm. daily gave persistently higher blood levels than 1,000 mgm. daily of chlortetracycline, and that owing to its slow excretion, the concentration of DMCT in the blood falls more slowly after administration is stopped than that of chlor- and oxytetracycline. DMCT was used for the treatment of 90 patients, the usual dose being 300 mgm. twice daily. They included 39 and 31 with infections of the air passages and urinary tract respectively and a miscellaneous group. Tabulated particulars are given, including exact diagnoses and results (recovery, improvement and no effect). There are some bacteriological data, but mostly unrelated to results. The authors were well satisfied, and consider that the small dose necessary should minimize side-effects: they saw only a few minor gastro-intestinal disturbances and 1 photo-sensitivity reaction. DMCT is contra-indicated in renal failure: in a uraemic patient the blood and urine concentrations were found to be almost exactly equal, whereas normally the latter is about 40 times higher. [This warning applies with at least equal force to most other antibiotics, and with greater force to those exerting toxic effects.]

L. P. Garrod

EISENBERG, G. M., WEISS, W., SPIVACK, A. P. & FLIPPIN, H. F. **Laboratory and Clinical Experience with Leucomycin, a New Antibiotic.** *Antibiotic Med.* New York. 1960, Sept., v. 7, No. 9, 546–52.

The minimum inhibitory concentration of leucomycin was determined for 3 groups of *Staphylococcus aureus*: 15 stock strains were all inhibited by 0·6 or 1·25 μgm./ml., as were 25 erythromycin-resistant strains (14 stock and 11 recently isolated); on the other hand, of 25 other recently isolated strains, 19 were inhibited by these concentrations and 1 by 20 and 5 not by 80 μgm./ml. [The sensitivity of these resistant strains to erythromycin is not stated.] Bactericidal concentrations were a large multiple (usually 32–128) of the bacteriostatic. 6 strains of group D streptococcus were inhibited by 0·3 or 0·6 μgm./ml.

Leucomycin, given orally in tablets, usually in doses of 400 mgm. at 6-hour intervals, was used in the treatment of 2 groups of patients. 10 had lung infections, the diagnosis of 9 being pneumonia and in 1 lung abscess: pneumococci were present in the sputum of all these patients [but nothing is said about their *in vitro* sensitivity to leucomycin]. The treatment was "effective"

but the results are described very briefly. Much more detail is given of the results in 17 cases of staphylococcal infection, mostly due to a type 80/81 strain, and classified as superficial infections (carbuncle etc.), deep suppuration (empyema etc.), and septicaemia or pneumonia or both. Leucomycin is described as having been "fairly effective" in this series: 2 patients died, and in those more severely ill the temperature seems to have fallen rather slowly. The staphylococcus was recovered from the lesion during or after treatment in 8 cases, and in 6 of these, the interval varying from 3 to 53 days, it had become resistant to 80 μgm./ml. One infant developed pancytopenia, from which it recovered when treatment was stopped.

L. P. Garrod

SIROTNAK, F. M., LUNT, Ramona B. & HUTCHISON, Dorris J. **Genetic Studies on Amethopterin Resistance in *Diplococcus pneumoniae*.** *J. Bacteriology*. 1960, Nov., v. 80, No. 5, 648–53. [15 refs.]

WEINSTEIN, L., MADOFF, M. A. & SAMET, C. M. **The Sulfonamides.** *New England J. of Med.* 1960, Oct. 20 & 27, Nov. 3 & 10, v. 263, Nos. 16, 17, 18 & 19, 793–800; 842–9; 900–907; 952–7. [257 refs.]

CUTTING, W., FURST, A., READ, Dorothy, GRANT, D., CORDS, H., MEGNA, J. & BUTTERWORTH, E. **Antiviral Extracts from *Proprionibacteria*.** *Antibiotics & Chemotherapy*. New York. 1960. Oct., v. 10, No. 10, 623–5.

"Fermentation extracts of *P. freudenreichii* contained antiviral activity against Columbia SK virus in mice. Reductions of mortality from rates of the order of 75 per cent. in the controls to 55 per cent. in treated animals were observed. The time at which one half the animals were dead was increased from 6 to 7 or 8 days. The active substance in the extracts has been called propionin."

NAUMANN, P. & WALZ, A. Zum gegenwärtigen Stand der chirurgischen Händedesinfektion. [**On the Future Position of Surgical Hand Disinfection**] *Deut. med. Woch.* 1960, Nov. 4, v. 85, No. 45, 1976–84, 2008, 3 figs. [13 refs.]

This paper is about "Rapidosept", which contains (in unstated proportions) dichlorbenzyl alcohol, isopropanol, glycerine, glycol derivatives and "regreasing lathering material". A quantity of 3 or 5 ml. is rubbed over the hands and forearms "with gentle washing movements" for a specified period. The effect of this and other treatments was tested by subsequently washing the hands in sterile water and cultivating the bacteria from this on a membrane filter. In 2 experiments employing many pairs of hands the average reductions in the counts produced by rapidosept, as compared with those from hands simply scrubbed with soap and water, were 97·89% and 96·22%. Treatment with 80% ethanol reduced the count by 97·55%. [There thus appear to be no clear grounds for preferring this new antiseptic to spirit although the authors evidently do so.] Disinfection by rapidosept is real and not only apparent: subsequent washing with soap or in ascites fluid does not release more bacteria as is the case after disinfection with a quaternary ammonium compound. There are photographs of cultures illustrating this. *L. P. Garrod*

FALLON, R. J. **Sterilisation of Radium Needles and Gynaecological Applicators.** *Lancet*. 1960, Nov. 19, 1133–5, 5 figs.

This paper describes ways in which radium needles and applicators may be sterilized by steam under pressure in a domestic pressure cooker. The needles are inserted in a special lead block with needle cavities extending right through its thickness to allow for free circulation of steam. Rubber cavity tubes and ovoids for gynaecological application are sterilized naked, the radium inserts of the tubes being moistened before assembly. Ovoids were totally immersed in the water of the pressure cooker. Experiments with *Bacillus stearothermophilus* spores showed that after 20 minutes at 121°C. (15 lb. per sq. in.) sterilization was achieved.

Protection against irradiation during the sterilization process is obtained by heating the cooker on an electric hot-plate which is placed on a trolley, the trolley top being surrounded by a wall of lead bricks. At the end of the sterilization process the whole trolley is wheeled into the theatre and the radium dispensed with long tongs. *J. C. Kelsey*

BRITISH STANDARDS INSTITUTION. **Specification for Pressure Steam Sterilizers of Small Size (with Independent Steam Supply) for Unwrapped Instruments and Utensils. B.S. 3233.** 10 pp. 1960. London: British Standards House, 2, Park Street, W.1. [4s.]

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

COMTOIS, R. D. **Changes in the Phage-Typing Patterns of Staphylococci following Lysogenization with a Related Group of Staphylococcus Bacteriophages.** *Canadian J. Microbiol.* Ottawa. 1960, Oct., v. 6, No. 5, 491–502. [20 refs.]

In several parts of the world strains of *Staphylococcus aureus* sensitive to phages 52 and 52A as well as to phages 80, 81 and 82 have been isolated together with strains of phage type 80/81. ASHESHOV and RIPPON [this *Bulletin*, 1959, v. 34, 1175] found that strains of type 80/81 when lysogenized with phages derived from strains of type 52/52A/80 became sensitive to phages 52 and 52A, thus becoming type 52/52A/80/81.

To study further the relationship between phages 52 and 52A and 80 and 81 the author has lysogenized each strain used for propagating phages 80, 81, 82 and KS6 with its homologous phage. In every case the resulting lysogenic strain displayed a new sensitivity pattern. Some strains lost their sensitivity to one phage to which they had formerly been sensitive. Some lost their sensitivity to one phage but at the same time became sensitive to phages 52 and 52A. Some became untypable. To give one example, a strain of phage type 80/81/82/KS6 when it was lysogenized with phage KS6 became type 52/52A/80/81/82, thus losing its sensitivity to KS6 (presumably owing to a straightforward prophage immunity reaction) but at the same time becoming sensitive to both phages 52 and 52A. In most cases the new pattern was stable and no reversion occurred on subculturing. No changes in antibiotic sensitivity were observed simultaneously with changes in phage type.

No strain could be lysogenized with phage 80, a failure also reported by ROUNTREE (*ibid.*, 1174), and the author thinks this may be because phage 80 is a virulent mutant of phage 52A, from which it was adapted.

The author suggests that untypable strains may occur in nature as a result of lysogenization. Untypable strains are often isolated from patients from whom strains of type 80/81 have also been isolated. He also suggests that lysogenization in nature could account for the appearance in hospitals of strains sensitive to phages 52 and 52A, as well as to the other phages, together with strains of type 80/81. *Janice Taverne*

ROGERS, H. J. & PERKINS, H. R. **5-Fluorouracil and Mucopeptide Biosynthesis by *Staphylococcus aureus*.** *Biochem. J.* 1960, Dec., v. 77, No. 3, 448–59, 9 figs. [46 refs.]

BLOBEL, H. & BERMAN, D. T. **Serologic Studies of Purified Staphylococcal Coagulase with special reference to Fluorescence Microscopy.** *J. Immunology.* 1960, Sept., v. 85, No. 3, 244–9. 2 figs. [11 refs.]

This paper describes experiments to demonstrate the specificity of staphylococcal coagulase and the use of fluorescent anticoagulase.

Coagulase purified by alcohol precipitation was used to immunize rabbits for the production of anticoagulase for cross inhibition tests, and an electrophoretically purified coagulase from a non-typable strain T was used to prepare serum for the fluorescent work. Gamma globulin after alcohol fractionation was labelled with rhodamine isothiocyanate and purified by absorption with anion-exchange resins followed by a coagulase-negative staphylococcus.

Labelled anticoagulase was used to stain 24-hour cultures of 57 strains of staphylococci. 3 of the 4 phage group 1 strains fluoresced weakly and 1 (type 52) showed no fluorescence. All 6 group II strains fluoresced, 4 of them strongly. Of the group III strains 8 fluoresced strongly, 2 weakly and 1 (type 53) failed to fluoresce. One of group IV and 3 in a miscellaneous group fluoresced strongly. 17 of 19 strains from bovine mastitis fluoresced strongly, one weakly and one not at all. There was no fluorescence with 8 of 13 coagulase-negative strains tested but one fluoresced strongly and 4 weakly [it is not clear if the phage types tested were all strains reacting only with one phage or if they were the propagating strains for these phages which in fact have a wider typing pattern].

Cross neutralization tests with unabsorbed sera prepared against strains of various types showed that there was, on the whole, higher cross neutralization between strains of the same phage group than between those of heterologous groups except for the 2 strains of Group I (types 29 and 52). Double diffusion precipitin analysis with a purified enzyme preparation from strain T reacted with its homologous antibody but the serum contained antibodies in addition to anticoagulase.

M. Patricia Jevons

BASS, J. A. & HIGGINBOTHAM, R. D. **Virulence of Staphylococci in Mice: a Comparison of Three Methods of Challenge.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 3, 364–78, 2 figs. [21 refs.]

The mouse virulence of various staphylococcal strains was tested by the intravenous route of challenge and the intraperitoneal route with and without mucin. 33 of the 40 strains of staphylococci tested were recently isolated from human lesions, the rest were various classical strains. All were coagulase positive.

Challenge doses consisted of 0·25 ml. of a suspension of 3–4-hour culture of organisms suspended in M/15 phosphate buffer (1×10^8 organisms). For intraperitoneal injections with mucin a 2-fold concentration of organisms was mixed with equal volumes of 10% mucin at *p*H 7·4. Results were recorded after 10 days' observation. Strains were also tested for α, β and δ lysin production, antibiotic sensitivity and phage type.

Results failed to suggest that virulence for mice was correlated with antibiotic sensitivity, phage type or, directly, with exotoxin production. 12 strains belonging to the 80/81 phage group were all poorly pathogenic by the intravenous route in contrast to the high virulence of the other 21 freshly isolated strains.

One method was not enough for the assessment of virulence. A strain could be highly virulent by one method and not by another. All strains produced α toxin in about the same amount but δ lysin production was variable. 14 strains were isolated from blood and these were highly virulent by intravenous challenge (median lethality 80%) although their α lysin production was not greater. 31 out of 40 strains were avirulent when injected intraperitoneally alone. The addition of mucin increased the lethality of the large majority of these to over 50% but the mortality of strains highly virulent on intravenous challenge was not raised above the level attained by intravenous injection.

The difference in the enhancing effect of mucin and the fact that the median time of death in the animals treated with mucin was 24 hours compared with 5 days in the mice challenged intravenously suggested that virulence by the 2 routes may be due to different factors.

M. Patricia Jevons

FISHER, S. **The Antistaphylococcal Activity of Human Sera *in vitro* and its Relationship to Passive Protective Potency.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Aug., v. 38, Pt. 4, 339–46. [14 refs.]

Human sera from blood donors showed some bactericidal and bacteriostatic effect when incubated with a suspension of a coagulase positive staphylococcus (strain Smith) for 15–16 hours at 37°C.

Aliquots of 8 sera with weak bacteriostatic action were pooled to make Pool 1 and 10 specimens with stronger bactericidal action combined to make Pool 2. Pool 1 was moderately bacteriostatic when tested against strain Smith, while Pool 2 was bactericidal, both unabsorbed and absorbed with zymosan. Pooled mouse serum was poorly bacteriostatic and gamma globulin was slightly less bactericidal than Pool 2. A single normal human serum F showed variations between bactericidal action and moderate bacteriostasis when tested against different staphylococcal strains.

When mice were injected subcutaneously with test sera and challenged the next day by intraperitoneal injection of the Smith strain with mucin, Pools 1 and 2 were similar in their protective power. Dilutions of between 1/3 and 1/27 covered the range from 90–100% survivors to 90–100% deaths. The protection was slightly less after absorption with zymosan. Gamma globulin had 20 times the protective activity of the pooled sera and one human serum from a case of recurrent boils had only slight mouse protective activity but was bactericidal at a dilution of 1/27.

There appeared to be no correlation between the ability of a serum to protect mice challenged by intraperitoneal injection and its ability to kill or limit multiplication of the same organism *in vitro*. *M. Patricia Jevons*

KOSUNEN, T. & WASZ-HÖCKERT, O. **Effect of Neomycin on Staphylococcal Infection in Mice.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 262–6, 2 figs.

"Neomycin, given subcutaneously to mice infected with Staphylococcus aureus, showed a high antibiotic activity evaluated by the microbial enumeration method from the kidneys."

FOX, E. N. & STEVENSON, D. **Effects of Trypsin on the Permeability of Streptococci.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 513–21, 5 figs. [26 refs.]

"Group A hemolytic streptococci exposed to low concentrations of trypsin for 30 min exhibited an increased permeability to various intracellular metabolites. Trypsin treated cells, after several washings, lost substantial quantities of magnesium and amino acids, including arginine. This loss was manifested in a decreased rate of glycolysis which could be returned to normal by the addition of magnesium and arginine or adenosine triphosphate to the medium in which the cells were metabolizing. Glycolysis by untreated streptococci was not stimulated appreciably by the supplementation of arginine, adenosine triphosphate, and magnesium ions. Trypsin treated streptococci incorporated radioactive amino acids into intracellular protein more readily than normal cells and the former synthesized more streptolysin O than normal streptococci in a media adequate for protein synthesis but not complete for cellular proliferation."

WAHL, R., CAYEUX, P. & DERLOT, E. Pouvoir pathogène particulier de streptocoques, à colonies rugueuses, du type 39 du groupe A. Étude immunologique de leurs extraits de Lancefield. **[Peculiar Pathogenicity of Group A, Type 39 Streptococci with Rough Colonies. Immunological Studies on their Lancefield Extracts]** *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 654–63, 3 figs. & 2 pls.

103 strains of streptococci isolated from the throats of 23 children in the course of long-term epidemiological study were found to produce curiously rough colonies on agar and to belong to type 39. Sublethal doses injected into mice often produced chronic suppurative lesions, which are uncommon with other streptococci. Gel diffusion tests suggested that there were 2 different antigenic fractions in the extracts. *R. E. O. Williams*

CROMARTIE, W. J., SCHWAB, J. H. & CRADDOCK, J. G. **The Effect of a Toxic Cellular Component of Group A Streptococci on Connective Tissue.** *Amer. J. Path.* 1960, July, v. 37, No. 1, 79–99, 12 figs. on 3 pls. [25 refs.]

Further study was made of the lesions resulting from intradermal injection of sonically disintegrated streptococci [see *e.g.* Schwab *et al.*, this *Bulletin*, 1959, v. 34, 679]. 3 principal variants of the nodular reaction, previously described, were observed: in 3 of the 36 animals

the lesions subsided in the period 2–12 days after the injection and did not recur; in 10 animals new lesions developed as the first batch of nodules were subsiding, up to 5 such exacerbations being seen in 45 days; and in 11 rabbits recurrences occurred after complete subsidence of the initial lesion, up to 53 days after the injection.

Histological preparations showed areas of inflammation characterized by separation of the collagen bundles and leucocytic infiltration. Later the collagen was replaced by material resembling fibrinoid. The chronic reaction showed infiltration by lymphocytes, macrophages and multinucleate giant cells.

Extracts of streptococci of groups B and D, and of *Streptococcus mitis* were also tested. A mild nodular reaction followed the injection of the group B extract in 4 animals, but none was seen with the others. Injection of living group A cells produced intense necrotic lesions. Repeated inoculation of group A extracts did not modify the reaction. *R. E. O. Williams*

Markowitz, A. S., Armstrong, S. H., Jr. & Kushner, D. S. **Immunological Relationships between the Rat Glomerulus and Nephritogenic Streptococci.** *Nature.* 1960, Sept. 24, v. 187, 1095–7, 4 figs.

Cultures of type 12 streptococci from nephritis patients were introduced into intraperitoneal chambers in rats and then removed after 3 days. The animals were examined at intervals for evidence of nephritis. Glomerular lesions were found in animals which had had mouse-passaged strains but not in those with unpassaged strains.

Streptococci of the strain producing this effect were extracted with trypsin and the extract was treated with trifluorotrichloroethane. Rabbits immunized with this material combined with Freund adjuvant yielded sera that produced some glomerular lesions when injected into rats. Similar "nephrotoxic" sera were produced in response to the injection of extracts of glomeruli made in the same way. *R. E. O. Williams*

Lacks, S. & Hotchkiss, R. D. **Formation of Amylomaltase after Genetic Transformation of Pneumococcus.** *Biochim. et Biophys. Acta.* 1960, Dec. 4, v. 45, No. 1, 155–63, 6 figs. [24 refs.]

Gerhardt, P. & Hedén, C. G. **Concentrated Culture of Gonococci in Clear Liquid Medium.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 49–51.

These authors' biphasic flask system consisted of a thick layer of medium solidified with 2% agar overlaid with a thin layer of liquid medium. The medium consisted of 1·5% proteose peptone No. 3, 0·2% dextrose, 1% soluble starch, 0·5% NaCL, 0·3% $Na_2HPO_4-2H_2O$ and 2% gelatin; final *p*H 7·3. Broth was clarified by adding Celite 512 and filtering; agar was added to 1% or 2%. Incubation took place in 10% CO_2 at 37°C. on a rotary shaker with a radius of 1¾ inches. Growth was compared with dextrose-starch broth overlay, that without starch, that without gelatin and that without either. Results are set out in a table [which is not easy to follow since the first 2 columns of figures are headed 24 hours and 48 hours respectively but the third states no time]. Growth occurred with the biphasic flask system which was several times more dense than with the usual method.

[Most pathologists find no difficulty in subculturing gonococci; what is difficult is the primary culture. It would be interesting to know how efficient this medium is for the latter.] *T. E. Osmond*

Metzger, J. F. & Smith, C. W. **Rapid Identification of *Neisseria meningitidis* by Fluorescent Antibody Technic.** *U.S. Armed Forces Med. J.* 1960, Oct., v. 11, No. 10, 1185–9. [23 refs.]

Rapid identification of *Neisseria meningitidis* is important for the selection of proper therapy. The authors describe a relatively simple method of identification by the fluorescent antibody technique with a polyvalent antiserum. Specificity was high, cross-reactions with 20 other *Neisseria* strains yielding only one slight reaction with a strain of *N. gonorrhoeae.* There was no specific staining with 107 other organisms.

Attention is drawn to the need for careful control of *p*H and tonicity of the staining solutions and mountant and the opinion is expressed that conjugated specific sera used directly are better for diagnostic work than fluorescein-labelled anti-species globulin used with the indirect technique [this *Bulletin,* 1959, v. 34, 265]. Such antiglobulins frequently contain other, acquired, antibodies which can lead to erroneous results. The need for full characterization of any serum used, not only against related bacteria but also against other species which may be present in the specimen, is emphasized.

The use of bovine serum albumin conjugated with lissamine rhodamine RB 200 as a counterstain eliminates non-specific fluorescence when smears of protein-containing material are examined and the authors believe that this technique could readily be applied to many problems in clinical diagnosis. *John R. Norris*

Veterans Admin. Dept. of Med. & Surgery. **Tuberculosis Laboratory Methods for the Veterans Administration-Armed Forces Cooperative Study on the Chemotherapy of Tuberculosis.** pp. iii+37, 1 fig. 1960, July. Wash. 25, D.C.: Central Office, U.S.A.

This monograph is very similar to the 1958 edition [this *Bulletin,* 1959, v. 35, 118]. There has been a little rearrangement of the 9 sections and there are few additions; sensitivity tests for kanamycin and thioamide are now included and the section dealing with identification of the mycobacterial species has been expanded.

There are 8 sections, which deal with the preparation and staining of specimens, the culturing of sputa, gastric contents, urine and testing for catalase, the testing for drug sensitivity, the homogenization and bacteriological examination of tissue, the identification of mycobacterial species, the safety measures that should be taken, the

maintenance and post-mortem examination of animals. The 9th section is the appendix which contains formulae of stains, media and various reagents.

[This edition reinforces the previous contention that this monograph is a valuable laboratory reference publication.] *S. R. M. Bushby*

TARSHIS, M. S. **Viability of the H37RV Strain of *M. tuberculosis* in Bovine Plasma Albumin and Charcoal Water Diluents after Varying Periods of Exposure at Room and Icebox Temperatures: a Note.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 1, 76–9. [10 refs.]

H37Rv was grown in Dubos medium for 7 days, and suspended in either 0·1% crystallized bovine plasma albumin in water or 0·01% decolorizing carbon in water. Viable counts were then made on both suspensions after intervals of 1 to 22 days at room temperature and at 5°C.

The counts showed that although the number of viable bacilli decreased progressively in both diluents the decrease was more rapid in the charcoal water; after 22 days the number of viable bacilli in the albumin solution had fallen to 30% at room temperature and to 8% at 5°C., whereas in the charcoal water they had fallen to 38% at room temperature and to 11% at 5°C. The survival was therefore less at 5°C. than at room temperature although during the first 2 days it was slightly better at the former temperature.

The bacilli showed no change in morphology, staining or virulence. *S. R. M. Bushby*

COHN, M. L., RUSSELL, W. F., Jr. & MIDDLEBROOK, G. **Effects of Carbon Dioxide and Daylight in culturing Tubercle Bacilli.** [Correspondence.] *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 579–80.

In this letter the writers report that a concentration of 2–5% carbon dioxide in the atmosphere is important in the cultivation of tubercle bacilli and that it is an essential factor in obtaining satisfactory growth with 7H–9 or 7H–10 solid medium. In the presence of this concentration of carbon dioxide these media are superior to Löwenstein-Jensen or ATS egg media, for the growth is more rapid and more luxurious; the transparency of the 7H–9 and 7H–10 media is also an added advantage. However, if either of these latter media are exposed to bright, but indirect sunlight for 36 hours they may no longer support the growth of tubercle bacilli.

S. R. M. Bushby

SANTOPADRE, G. & DELLE SEDIE, P. F. **Bacteriological Aspects of the So-Called Tuberculomas of the Lung.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 2, 97–114. [39 refs.]

In a careful search of the literature for the results of bacteriological examination of tuberculomas, the authors found that 24 groups of workers had reported on a total of 1,500 lesions. Of these lesions only 167 could be definitely identified as true tuberculomas, and only 52 were given a comprehensive bacteriological examination. The reports of these 52 examinations show that many of the lesions contained bacilli that could not be grown. [The data from this search are presented in 2 tables.]

The authors have examined 22 resected tuberculomas from 13 subjects in Leghorn, Italy, and in this paper they compare the results of the bacteriological examination of these lesions with the results of the examination of sputum, bronchial lavage and gastric juice obtained before the operation. [Very little technical detail of the examination is given and the results are presented in tables.]

50% of the tuberculomas contained no acid-fast bacilli in direct smears, but tubercle bacilli were grown from 3 of these; tubercle bacilli were grown from all the smear-positive specimens except 1 which was also negative by guineapig inoculation. 6 of the culture-positive tests were negative by guineapig inoculation and 2 were negative by culture but positive by guineapig inoculation. In the majority of the positive cultures from the lesions, the number of colonies grown was less than expected from the number of bacilli in the smear, and most of them took several months to grow; this discrepancy did not apply to the specimens taken before the operation. In general, the isoniazid-resistance and the streptomycin resistance of the bacilli from the lesions were similar to the resistance in the pre-operation samples, but the bacilli from the lesions tended to be more sensitive to PAS. There was poor agreement between low catalase activity and pathogenicity, although low catalase activity was usually associated with high isoniazid resistance; cytochemical test for virulence and the guineapig test gave good agreement.

The results are discussed at some length but the question of the viability of the majority of the bacilli in these lesions is left in doubt.

[This is a difficult paper to follow, firstly because of the style of English, and secondly because of its unusual form of presentation.] *S. R. M. Bushby*

WAYNE, L. G. **The Bacteriology of Resected Tuberculous Pulmonary Lesions. II. Observations on Bacilli which are Stainable but which cannot be Cultured.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 370–77, 3 figs. [13 refs.]

The results reported in this paper are a part of a 6-year study of the state of viability of stainable bacilli in specimens resected from human tuberculous lungs [this *Bulletin*, 1957, v. 32, 82]. The object of these investigations was not to obtain a slight increase in the number of positive cultures from these specimens but to obtain a dramatic recovery of viable bacilli, and in this respect the author admits failure.

The methods consisted of:—(1) adding activated charcoal to the lung homogenates; (2) freezing and thawing the tissues before grinding and suspending the homogenates in nutrient broth and incubating the cultures for 9 months; (3) first incubating the homogenates in Dubos-Tween 80-albumin broth; (4) using the method in which the lower portion of a Löwenstein-Jensen medium slope is bathed in Dubos medium and the culture is tipped

every 3rd week to re-inoculate the slope; (5) adding separately through diffusion phthiocol and pyruvate to Löwenstein-Jensen medium; (6) re-inoculation of negative slopes of Löwenstein-Jensen and Petragnani medium to fresh slopes of Löwenstein-Jensen medium; (7) incubating for periods up to 2 years; (8) modifying the gaseous environment so that it contained 50% oxygen or 5% oxygen in nitrogen, or a mixture of 16% oxygen, and 20% carbon dioxide in nitrogen. Inoculation of the homogenates into guineapigs by the intratesticular and intracardial routes, and the subcutaneous route, with and without powdered silica, were also unsuccessful; the giving of the animals daily doses of 2·5 mgm. of cortisone was similarly without effect.

In an attempt to determine the effects on the stainability of tubercle bacilli of prolonged incubation under anaerobic conditions, 17 homogenates of lung tissue containing bacilli were incubated under sterile mineral oil for 2 years. At the end of this period the bacilli were found to be still demonstrable by smear in 16 of the specimens although the number of bacilli had decreased to about 10% of the original number. The autolytic capacity of tubercle bacilli of a Dubos culture was also determined in an atmosphere of carbon dioxide or in the presence of 20 μgm. streptomycin per ml., and lysis was found to be more rapid when the bacilli were in the phase of active growth.

The incidence of smear-positive, culture-negative resection specimens was found not to be related to the interval between sputum-conversion and resection, although as the interval increased the incidence of culturable bacilli decreased. Therefore although after conversion the bacilli steadily lose their ability to multiply in culture they do not disappear from the tissues, and in spite of the author's failure to grow them, they have not yet been shown to be dead. *S. R. M. Bushby*

Arima, J., Yamamoto, K. & Takahashi, Y. Comparaison de la méthode de la culture de tissus avec les quatre méthodes conventionnelles pour l'évaluation de la virulence des bacilles tuberculeux. **[Comparison of the Method of Cultures in Tissue and the 4 Conventional Methods for estimating Virulence of Tubercle Bacilli]** *C. R. Soc. Biol.* 1960, v. 154, No. 4, 883–7.

In a comparison of 3 methods of assessing virulence, using 9 laboratory strains and 29 recently isolated strains of tubercle bacilli, the authors found that their method of assessing virulence by the increase in the number of tubercle bacilli in the spleen 5 days after intravenous injection [this *Bulletin*, 1960, v. 35, 181] gave slightly better agreement with that based on the extent of disease in guineapigs, 8 weeks after the subcutaneous injection of the bacilli, than that which uses the survival time of mice after intravenous injection. Agreement between the spleen culture method and the usual guineapig test was found with 26 strains as compared with 20 strains with which there was agreement between the spleen culture and the mouse test, and with 24 with which the guineapig test and mouse tests agreed.

The neutral red test and ability to form cords showed poor agreement with these animal tests.

S. R. M. Bushby

Takahashi, Y. & Onodera, T. Tuberculose expérimentale et existence de trois anticorps différents, antipolyoside, antiprotéide et antiphosphatide. **[Experimental Tuberculosis and Existence of 3 Different Antibodies, Antipolysaccharide, Antiprotein and Antiphosphatide]** *C.R. Soc. Biol.* 1960, v. 154, No. 4, 887–9, 1 fig.

By using red cells sensitized with polysaccharide, protein and phosphatides from the tubercle bacilli the development of antibodies was followed in rabbits injected with 1 mgm. BCG and 1 mgm. of virulent human tubercle bacilli by the subcutaneous and intravenous routes; the development of the antibodies was followed for 12 weeks.

In each of the animals the highest titres were reached by the antibodies to the polysaccharides (1:320) but the concentration of the antibodies decreased after about the 5th week except in the animals injected intravenously with the human strain; the antibodies to the proteins were of lower concentrations but tended to follow those for the polysaccharide. Concentrations of the antibodies for the phosphatides were very low in the animals injected subcutaneously with both strains; in the animals injected intravenously with BCG the titres reached to 1:60 in the 7th week, but they then fell, whereas in the animals injected with the human strain, the titres continued to rise to reach a maximum of 1:160. Treatment with streptomycin or isoniazid had little effect on formation of antibodies to the polysaccharide or the protein but it depressed the formation of those to the phosphatide.

From these results the phosphatides are considered to be situated more deeply within the bacillus than are the other 2 antigens, and antibody stimulation to be dependent on their release through destruction of the bacillus; the concentration of antibodies to the phosphatides therefore, is more closely parallel to the course of the disease. *S. R. M. Bushby*

Youmans, Anne S., Youmans, G. P. & Hegre, A., Jr. **Effect of Homogenates of Organs from Immunized Guinea Pigs on the Respiration of *Mycobacterium tuberculosis*.** *J. Bacteriology.* 1960, Sept., v. 80, No. 3, 394–9, 2 figs. [14 refs.]

The organs homogenized were the lungs and spleens of guineapigs immunized with either 5 mgm. or 1 mgm. of BCG, the homogenization being done in 4 ml. 0·01 M phosphate buffer, per gm. of tissue. The effects on the respiration of H37Rv were determined in the Warburg apparatus and as the homogenates of the lungs from unvaccinated guineapigs increased the respiration, but to a lesser extent after dialysation for 18 hours in Cellophane sacs, all the homogenates were dialysed. Groups of 5 animals were used.

Homogenates from the lungs of guineapigs removed at intervals up to 6 weeks after vaccination increased the respiration to the same extent as those from unvaccinated animals, but with those from animals vaccinated 8 weeks previously the increase was less. When the interval after vaccination was extended to 12 weeks the homogenates then caused a decrease in respiration, and

although the individual variation between the animals was fairly wide, the differences between them and the control animals were highly significant; the Qo_2 for the animals vaccinated with 5 mgm. were −0·30, −0·32, −0·36, −0·40, and −0·30; for those vaccinated with 1 mgm. they were −0·14, 0·68, −0·20, −0·16 and 0·10; and for the unvaccinated they were −0·28, 0·72, 1·16, 0·88 and 0·76. The depression also occurred with animals killed after 23 and 27 weeks. The pattern of inhibition of the endogenous respiration varied; the inhibition was in some instances immediate but with others it was delayed for 1½–2 hours, and leaving the homogenates to steep for 3 days at 4°C. slightly increased the inhibition.

Homogenates of the spleens behaved similarly although somewhat more variably than did those of the lung. Inhibitory homogenates were also shown to inhibit the oxidation of lactate and pyruvate, thus providing direct evidence of the presence of a respiration-inhibitory substance, but all attempts to separate this substance from that present in normal homogenates which increased endogenous respiration were unsuccessful.

The authors emphasize the need for caution in attaching too much significance to these findings in relation to the mechanism of acquired immunity in tuberculosis.

S. R. M. Bushby

Weiss, D. W. & Wells, A. Q. **Vaccination against Tuberculosis with Nonliving Vaccines. III. Vaccination of Guinea Pigs with Fractions of Phenol-Killed Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 339–57. [53 refs.]

In these experiments groups of guineapigs were injected with either the methanol extract of tubercle bacilli killed with phenol and washed with acetone or the bacillary residues and challenged with bovine tubercle bacilli, the survival time being compared with those of unvaccinated guineapigs and those vaccinated with BCG. The methanol extraction method was that previously described [this *Bulletin*, 1960, v. 35, 920].

In the first experiment the mean survival time of the animals injected with 3 mgm. of the extract was 55 days, those injected with 10 mgm. was 36 days, those injected with living BCG was 63 days, and the control animals 33 days; these times were calculated from the day of challenge which was 35 days after the day of vaccination. Of the animals injected with the 3 mgm. of the extract only 2 became tuberculin positive, whilst all those given 10 mgm. or the BCG converted.

In the second experiment in which 19 groups were vaccinated none of the 12 groups given the methanol extract alone showed a significant prolongation of life, except a group given 3 mgm. suspended in Freund's adjuvant, although when the extract was given with 0·3 mgm. of the residue there was a significant increase in the mean survival time.

The remainder of the paper is concerned with unsuccessful attempts to account for the disappointing variability of the protection afforded by the extract in these animals seeing that it gave high promise in mice [*ibid.*, 1956, v. 31, 745]. The immunogenic powers of the bacillary residue were consistently shown to be of an order similar to that of living BCG but this immunity, in contrast to that produced by the extract, was associated with tuberculin hypersensitivity.

[The results of these experiments are extensively discussed and those especially interested in vaccination with extracts of tubercle bacilli should read the original article.]

[See also *ibid.*, 1960, v. 35, 460]. *S. R. M. Bushby*

Peizer, Lenore R., Chaves, A. D. & Widelock, D. **Characteristics of Mycobacterial Populations found in the Sputum of Tuberculous Patients after Prolonged Isoniazid Therapy.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 568–73, 1 fig. [11 refs.]

These studies were made on 46 positive cultures from sputa from 50 patients. Most of these patients were males of an average age of 55 years, who had been treated continuously for at least 2 years with isoniazid, either alone or in combination with other antituberculous drugs. The sensitivity tests were made directly from the sputum homogenate and from the drug-free control culture; catalase tests and guineapig inoculations were also made from the control tubes.

The cultures could be classified into 5 types according to their virulence:— (1) virulent and of high catalase activity, but of variable isoniazid resistance, ranging from susceptibility to 1 μgm. per ml., to resistance to 25 μgm. per ml., and tending to be less resistant when recovered from the guineapig; (2) virulent, and of moderate catalase activity, but of variable isoniazid resistance which did not change during passage through the guineapig; (3) low virulence producing no progressive disease, and of low catalase activity, but of variable isoniazid resistance and tending to be more resistant when recovered from the guineapig; (4) these strains differed from the 3rd group by the resistance being unaltered when recovered from the guineapig; and (5) these strains differed from the 3rd and 4th groups in being of such low virulence that they could not be recovered from the guineapig.

No correlation was found between the course of the disease and the characteristics of the bacilli; at the end of the study, 6 of the patients had died from causes other than tuberculosis, 9 from tuberculosis, and 31 were still alive and continuing treatment with isoniazid.

S. R. M. Bushby

Viallier, J. & Cayré, R. M. Étude de 23 souches de *Mycobacterium tuberculosis* var. Bovis, isolées de lésions humaines: Thermosensibilité, production de niacine. Evolution ultérieure. [**Study of 23 Strains of *Mycobacterium tuberculosis* var. *bovis*, isolated from Human Lesions: Thermostability, Production of Niacin. Subsequent Evolution**] *C.R. Soc. Biol.* 1960, v. 154, No. 3, 652–4.

Of 624 strains of tubercle bacilli isolated from pathological specimens, 28 were identified as the bovine variety by their higher pathogenicity for the rabbit; 2 were of 139 strains from sputa, 4 of 116 strains from cerebrospinal fluid, 18 of 51 strains from cervical glands, 1 of

the 32 strains from various specimens, *e.g.*, tissue, urine or ascitic fluid, and all 3 of the strains taken from the gums. None was found among 265 strains from gastric lavage or 18 from pleural fluids.

Samples of milk were infected with 2 concentrations of 23 of these bovine strains, 1 being 50 times weaker than the other [the actual concentrations are not stated]. Heating the milk at 62°C. for 30 minutes killed all the bacilli but heating for 15 seconds at 71°C. was less efficient, for bacilli were recovered from the samples of milk containing the weaker concentration of 2 of the strains and from samples containing the stronger concentration of 15 of the strains. In order to test the effects of lactic acid fermentation on the survival of the bacilli, samples of milk were infected with the 23 strains, left at room temperature and cultured at intervals; the survival of the bacilli depended upon the size of the inoculum; with the heavier inocula 11 of 16 samples were positive after 8 days but only 1 was positive after 15 days.

Of the 28 strains, 27 were niacin-negative and the 1 positive strain was a little weaker than the human strains. When 23 of these strains were retested for virulence, 1–6 years after isolation, 18 were still virulent for the rabbit and 22 for the guineapig; 1 of the strains had assumed the characteristics of an atypical non-chromogen, insensitive to isoniazid and catalase-positive.

S. R. M. Bushby

VIALLIER, J., CAYRÉ, R. M. & AUGAGNEUR, J. Evolution lointaine des caractères de souches de *Mycobacterium tuberculosis* " isoniazido-résistantes ". [**Long-Term Changes in the Characters of the Strains of Isoniazid-Resistant *Mycobacterium tuberculosis***] *C. R. Soc. Biol.* 1960, v. 154, No. 3, 655–6.

10 strains of isoniazid-resistant tubercle bacilli, isolated more than 4 years ago and repeatedly subcultured for 30 months in media containing 20 μgm. isonazid per ml. and then for 14 months in isoniazid-free media, retained the characteristics of human tubercle bacilli; they were still non-pigmented, neutral-red positive, catalase-negative, niacin-positive, reductase-negative and sensitive to α-ethylthio*iso*nicotinamide. It would seem therefore that if prolonged contact with isoniazid can induce the change of typical tubercle bacilli to atypical mycobacteria, then the occurrence must be rare. *S. R. M. Bushby*

CANETTI, G., GRUMBACH, F. & GROSSET, J. **Studies of Bacillary Populations in Experimental Tuberculosis of Mice treated by Isoniazid.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 295–313, 5 figs. [38 refs.]

Mice were injected intravenously with 2 recently isolated strains of tubercle bacilli and 14 days later treatment was started with a daily oral dose of either 0·1 mgm. or 1·0 mgm. of isoniazid for 20 weeks. At day 0, and on the 14th, 35th, 70th, 105th and 140th day, 3 of each group were killed. Serial dilutions of homogenates of their spleens and lungs were inoculated onto Löwenstein-Jensen medium containing concentrations of isoniazid ranging from 0·05 to 100 μgm./ml.; colony counts were made from the 25th to the 50th day of incubation. The concentration of isoniazid in the blood 2 hours after a third daily dose of 0·1 and 1·0 mgm. of the drug was also determined.

Only the results with the lungs are reported in detail and as the results with the 2 strains of tubercle bacilli were very similar they are presented together. They are given in tabular and graphic form and show that whereas the higher dose of the drug caused a 90% fall in the bacillary count within 14 days of treatment, a comparable fall with the smaller dose took 70 days, in spite of the fact that the mice on this lower dose had the tuberculocidal concentration of 0·25–0·5 μgm. isoniazid per ml. in the blood 2 hours after dosing. The fall in the bacillary population of the animals treated with the higher dose was due not only to a reduction in the fully sensitive bacilli but also in those resistant to up to 1 μgm./ml., and in these mice it was not until the 70th day that the development of highly resistant bacilli caused an increase in total population. In the animals treated with the lower dose the fall in the bacillary count was mainly due to a reduction in the isoniazid-susceptible population, but there was, however, a big individual variation among the mice and by the 140th day there was in general little difference in the number of highly resistant bacilli in the 2 groups in spite of the animals given the higher dose of isoniazid having concentrations in the blood of 2–4 μgm./ml.

In the long discussion the authors endeavour to explain their unusual recovery of resistant variants from mice and they discuss the value of administering high doses of isoniazid. *S. R. M. Bushby*

AUDRIN, J. Mise au point d'une méthode de mesure de la sensibilité des bacilles tuberculeux aux antibiotiques présents dans le sérum des malades. [**Description of a Technique to evaluate the Sensitivity of Tubercle Bacilli to Antibiotics present in Patients' Sera**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 757–66.

In a preliminary experiment, bovine serum in concentrations up to 50% in Jensen medium added before coagulation by heating for 20 minutes at 84°C., did not adversely affect the growth of H37Rv, and the results of further experiments showed that the inhibitory power of the serum of patients on isoniazid, dihydrostreptomycin or PAS could be determined by adding 1 ml. of decreasing dilutions of the serum in bovine serum to 5 ml. of Jensen medium; 2 hours after the injection of 500 mgm. isoniazid and 1 gm. of dihydrostreptomycin the inhibitory titres were 1/200–1/400 and 1/60–1/120, respectively.

The method can also be used for determining the sensitivity of the patient's strain of tubercle bacilli by comparing the inhibitory titre of the serum for H37Rv and for the patient's autogenous strain. *S. R. M. Bushby*

WALTER, A. M., OTTEN, H., YAMAMURA, Y. & BLOCH, H. **Bacterial Populations in Experimental Murine Tuberculosis. III. Chemotherapeutic Studies.** *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 213–23, 8 figs. [20 refs.]

The object of this study was to compare the effects of various chemotherapeutic drugs on the total bacillary

population of mice infected intravenously with H37Rv, the total number of bacilli being determined by homogenizing the whole animal by the method previously described [this *Bulletin*, 1960, v. 35, 1134]. Treatment with the drugs was started before and at various stages during the infection, and some of the mice of each group were killed at intervals. In untreated mice, an initial drop in the number of viable units occurs, presumably owing to aggregation of the bacilli within the capillaries of the lung, but about 1 week after infection there is a marked increase which is preceded by a fall in bodyweight of the animals. 4 experiments, differing in the virulence of the infection and in the drugs used, are described.

The course of the tuberculosis in mice can be divided into 4 phases; in the first phase the bacilli are extracellular and stimulate a cellular reaction; in the second, the bacilli are intracellular and then only drugs that can readily enter the cells would be expected to affect their multiplication; in the third, the bacilli become extracellular due to destruction of the cells and then all antituberculous drugs ought to affect multiplication; and finally the bacilli multiply both extracellularly and intracellularly and also in the necrotic tissues. The results of the experiments only partly fulfilled these expectations for although isoniazid, 20 mgm. per kgm., affected multiplication at all stages after the preliminary lag phase, streptomycin, which penetrates cells very poorly, in doses of 25 and 250 mgm. per kgm., showed a maximum effect during the third phase in the first experiment, but in the other experiments the difference between its early and late administration was less pronounced. Pyrazinamide, 500 mgm. per kgm. and thioamide, 30 mgm. per kgm. behaved similarly to isoniazid, and thiocarbamide, 50 mgm. per kgm., which poorly penetrates cells, to streptomycin. With isoniazid the bodyweights of the mice reflected accurately the changes in the bacillary population, but with the other drugs this inverse correlation was less consistent.

Triton WR 1399, given subcutaneously in doses of 180 mgm. per kgm., on the first, fourth and seventh day had no effect on the multiplication of the bacilli but the animals gained weight. *S. R. M. Bushby*

Acred, P., Brown, D. M. & Wright, D. **The Antitubercular Activity of 3-Acetylthiopropylene Sulphide and 3-(2-Furoylthio)Propylene Sulphide.** *Brit. J. Pharmacol. & Chemotherapy.* 1960, Dec., v. 15, No. 4, 496–9, 1 fig.

"Two derivatives of 3-mercaptopropylene sulphide (B.R.L. 482), 3-acetylthiopropylene sulphide (B.R.L. 459) and 3-(2-furoylthio)propylene sulphide (B.R.L. 658), have been tested in mice for antitubercular activity. The compounds were administered daily in arachis oil by the subcutaneous route. When tested by a prolongation in survival time B.R.L. 459 was less active than streptomycin, while B.R.L. 658 was of the same order of activity. When assessed by the lesions present in the lungs after 14 days' treatment B.R.L. 658 was as active as isoniazid and B.R.L. 459 was of the same order of activity as streptomycin. Neither compound, however, cured an established infection and resistance developed rapidly to both compounds, both *in vitro* and *in vivo*. It is concluded that, in view of their adverse physical and pharmacological properties, the compounds are unsuitable for clinical use."

Gross, P., Westrick, Marian L. & McNerney, J. M. **The Pulmonary Response to Tuberculin.** *Arch. Pathology.* 1960, Aug., v. 70, No. 2, 233–43, 9 figs.

40 guineapigs were injected with 0·1 ml. 1 : 100 dilution of a 6-week Dubos-Middlebrook culture of human tubercle bacilli and 22 other guineapigs were similarly treated but with an undiluted 8-week culture; when tested 3 weeks later all the animals were sensitive to 0·005 mgm. of PPD. 25 of the animals which had been given the diluted culture were then injected intratracheally with 0·005 mgm. PPD and 2, 6, 12, 18 and 24 hours later pairs of them were killed, unsensitized guineapigs which were also given PPD, being killed at the same time; the other 15 guineapigs that had been given the PPD intratracheally were killed at intervals from 5 to 11½ months. The remaining 15 guineapigs that had been sensitized with the diluted culture were given intratracheal injections of 0·005 mgm. of PPD every month for 6 months and killed at intervals from 3 to 12 months. The animals sensitized with the undiluted culture were injected intratracheally with 0·01 mgm. PPD, and groups of them were killed at 8 hours, 1, 2, 7, 14 and 28 days. Sections of the lungs were stained with haematoxylin and eosin and photographed; the sections were then decolorized, restained for reticulin stroma and the same microscopic fields re-photographed. The paratracheal lymph nodes were also examined.

The basic tuberculin response in the lungs was evident at 2 hours, and it consisted of proliferation of alveolar cells with associated propagation of reticulin fibres, which sometimes obliterated the alveoli. There was also an eosinophilic infiltration and the appearance of alveolar macrophages and multinucleated giant cells in the airspaces. With adequate sensitization or dosage of tuberculin, the exudation of alveolar fluid masked this basic effect, but by the end of a week these exudative features had mainly subsided and the basic response remained discernible for months. At no stage did collagen develop. With insufficient sensitization the pulmonary response to tuberculin was indistinguishable from that in non-sensitized animals.

In the lymph nodes granuloma-like clusters and masses of eosinophilic reticulo-endothelial cells, not usually associated with reticular fibres, developed in the reacting animals; these changes persisted for as long as 5 months.

The basic chronic reaction of the pulmonary tissue was not considered specific, mainly because a few spontaneous lesions found in apparently normal stock resembled the residual lesions, but also because eosinophilic infiltration and pneumonitis have been found in animals that have inhaled various dusts. The observations are discussed in relation to those of other workers. *S. R. M. Bushby*

Ponzoni, R. Paini, A. & Bisbini, P. Ricerche sperimentali sulla fosfatasi, ureasi e fermentazione della destrina quali tests per la identificazione del *C. diphthriae*. [**Experimental Investigations on Phosphatase, Urease and Dextrin Fermentations as Tests for the Identification of *C. diphtheriae***] *Ann. Sclavo.* Siena. 1960, July–Aug., v. 2, No. 4, 329–46. [31 refs.] English summary.

In view of the large number of non-toxic *Corynebacterium diphtheriae* which appear at the present time and the possibility emphasized by recent work of the action of bacteriophage in converting non-toxigenic to virulent strains, the authors have examined afresh some of the biochemical activities of the corynebacteria in order to determine their value in making a differentiation between non-toxic diphtheria strains and diphtheroid bacteria. In their series, 102 pathogenic strains of *C. diphtheriae* and 44 non-toxic strains were found to be negative by the phosphatase test while 84 strains described as *C. pseudodiphtheriae* were found positive. [This finding is at variance with earlier work of Zangaglia and Ferrata (this *Bulletin*, 1956, v. 31, 667), who agreed in finding that all true diphtheria strains are negative by this test, but diverged in showing 21 of 30 diphtheroid strains giving positive results.]

There is no attempt to correlate the findings with much British and German work on the value of blood tellurite media in differentiating diphtheria and diphtheriod strains.

[In the author's summary in English, *C. diphtheriae* is incorrectly stated to be phosphatase positive. This error does not occur in the Italian or French summaries.]

J. W. McLeod

Narbutowicz, Barbara. Działanie substancji powierzchniowoczynnych na konwersje toksyczności maczugowców błonicy. [**The Effect of Surface-Active Agents on the Lysogenic Conversion to Toxigenicity of *Corynebacterium diphtheriae***] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 3, 221–30, 8 figs. on 4 pls. [10 refs.] English summary.

An investigation has been made of the effect of 8 surface-active agents on the lysogenic conversion of *Corynebacterium diphtheriae* to toxigenicity by phage. Broth containing the agent to be tested was inoculated with an 18-hour culture of *C. diphtheriae* strain 444 and incubated for 1 hour at 37°C. Phage 25 was then added and incubation was continued for 24 hours. Toxigenicity was then tested in guineapigs. Conversion to toxigenicity took place in the presence of 2·5% saponin and digitonin, but was inhibited by 0·1% Tween 80 and 4 other proprietary products in concentrations of 0·0025–0·06%. The multiplication of the phage was reduced by saponin and completely inhibited by the other agents; the phage was inactivated by all agents in the concentrations tested after 24 hours at 37°C., but the growth of *C. diphtheriae* was not affected.

D. J. Bauer

Strauss, N. **The Effect of Diphtheria Toxin on the Metabolism of HeLa Cells. II. Effect on Nucleic Acid Metabolism.** *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 351–9, 4 figs. [11 refs.]

In an earlier investigation with Hendee [this *Bulletin*, 1959, v. 34, 658] the author has shown that a rapid interference with protein synthesis occurs in tumour cells growing in artificial culture if they are exposed to relatively small concentrations of diphtheria toxin.

In this paper the results of similar investigations on the effect of diphtheria toxin on the synthesis of nucleic acids and acid soluble organic phosphates are examined. The cultures of the HeLa cells had preparations of uridine and thymidine or orthophosphate placed at their disposal, all three substances being labelled with P^{32}. No effect corresponding to that on protein synthesis was observed. A rapid suspension of the building of nucleic acid or of the synthesis of nucleoside phosphate under the influence of diphtheria toxin was not found in such experiments. The early disintegration of the culture cells under the action of diphtheria toxin, it is suggested, may be explained by (a) inhibition of protein synthesis, or (b) the disintegration of the cell membrane.

The evidence for the relative validities of these two hypotheses is discussed. *J. W. McLeod*

Rogers, K. B., Zinnemann, K. & Foster, W. P. **The Isolation and Identification of *Haemophilus* spp. from Unusual Lesions in Children.** *J. Clin. Path.* 1960, Nov., v. 13, No. 6, 519–24. [24 refs.]

During routine bacteriological investigations *Haemophilus influenzae* was isolated from several unusual sites in children: from blood cultures after tonsillectomy or tonsillotomy in 5 cases; from the urinary tract in 8 cases; from the lumen of 15 of 376 vermiform appendices; from osteomyelitis and pyarthrosis in 6 cases; and from 2 perianal abscesses, 3 paronychiae, 1 infected thyroglossal cyst, and several skin infections.

Of the organisms present in the throat before removal of the tonsils, *H. influenzae* was the only one isolated from post-operative blood cultures. It is suggested that *H. influenzae* bacteraemia is more common than supposed and precedes skeletal and urinary tract infection. Injury or congenital abnormalities may determine the site of infection; of the 8 children with urinary tract infection 2 had suffered recent violent injury and 5 had congenital abnormalities of the urinary tract. [The isolation of *H. influenzae* from the urine of a child with an apparently uncomplicated first attack of pyelonephritis should stimulate search for congenital abnormalities.] Infection of the appendix, perianal abscesses, paronychiae, and skin infections probably follow direct contamination or passage of the organism through the gut. Similar infections would probably be more widely recognized if routine bacteriological investigation allowed the isolation and identification of *H. influenzae*. *A. C. Scott*

Thornley, Margaret J. **The Differentiation of *Pseudomonas* from other Gram-Negative Bacteria on the Basis of Arginine Metabolism.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 37–52. [39 refs.]

Ewing, W. H., Davis, Betty R. & Edwards, P. R. **The Decarboxylase Reactions of Enterobacteriaceae and their Value in Taxonomy.** *Pub. Health Lab.* 1960, July, v. 18, No. 4, 77–83.

Moller (*Acta Path. et Microbiol. Scandinavica,* 1955, v. 36, 158) described a basal medium to which 1% amino acid was added, the medium being covered with a layer of liquid paraffin. The authors report the reactions of 2,937 strains of the enterobacteria in L-lysine, L-arginine and L-ornithine.

	Lysine	Arginine	Ornithine
Escherichia coli	+or−	(+) or−	+or−
Shigella sonnei	−	−	+
Other shigellas	−	−	−
Salmonella typhi,			
S. gallinarium	+	−	−
S. paratyphi A	−	(+)	+
Other serotypes	+	(+)	+
Arizona	+	(+)	+
Citrobacter	−	(+)	−
Klebsiella	+	−	−
Aerobacter A	−	+	+
B	+	−	+
C	+	−	+
Hafnia	+	−	+
Serratia	+	−	+
Proteus vulgaris	−	−	−
P. mirabilis	−	−	+
P. morganii	−	−	+
P. rettgeri	−	−	−
Providence	−	−	−

[This table is a modified version of the authors' Table 2, based on their Table 1.]

The results [see table, where (+) indicates a delayed positive reaction] show that the tests have value in distinguishing different members of the enterobacteria. [The use of the name Aerobacter for MR− VP+ motile organisms is confusing to those not familiar with the sinuous progress of the taxonomy of the family Enterobacteriaceae. Aerobacter A=*Enterobacter cloacae*; Aerobacter B=*Enterobacter aerogenes*; and Aerobacter C=*Enterobacter liquefaciens.*]

A comparison of Moeller's medium with a modification by Falkow [this *Bulletin,* 1959, v. 34, 564] showed that the media gave similar results except with Klebsiella, Aerobacter and Proteus group cultures. On the whole Moeller's medium was more reliable and is recommended as a standard of reference. *S. T. Cowan*

Le Minor, L. & Edwards, P. R. Présence de trois phases de l'antigène flagellaire chez des bactéries du groupe *Salmonella.* [**Existence of Three Phases of the Flagellar Antigen in Bacteria of the *Salmonella* Group**] *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 469–74, 1 fig.

This paper describes the isolation from the lymph node of a pig and from a diseased turkey-poult, respectively, of two salmonella strains having the same, but hitherto undescribed, characters. Preliminary investigation placed these two cultures in the Kauffmann-White O-group E_2 as monophasic organisms with the antigenic formula 3,15: z_{27}. Further study of the cultures by growing them in semi-solid agar containing z_{27} antiserum revealed the presence of 2 further phases or forms—one with the antigenic formula 3,15:e,h, and the other, 3,15:1,2—which were spontaneously reversible each to the other. It was still possible, but only with difficulty, to obtain the form 3,15:z_{27} from the form 3,15: 1,2. Although this is the first published record of the recognition of three naturally occurring flagellar phases in a *Salmonella* culture, it is understood that other workers (personal communications) have made similar observations. *H. J. Bensted*

Ghatak, S. **Dehydrogenation of Amino Acids, Carbohydrates and Organic Acids by *Salmonella typhosa.*** *Indian J. Med. Res.* 1960, May, v. 48, No. 3, 347–55, 4 graphs. [23 refs.]

Using triphenyl tetrazolium chloride for this study of the dehydrogenases, the author found that resting cells of typhoid bacilli were capable of dehydrogenating a number of substrates. The carbohydrates showed the best dehydrogenation, followed by the metabolic intermediates of the tricarboxylic acid cycle. The amino acids showed somewhat less enzyme activity. Bacterial cell-free extracts were less active than actual cell suspensions. Although all strains of *Salmonella typhi* showed activity there was a good deal of variation in intensity, but the activity could not be correlated either with mouse-virulence or antigenic structure.

The characterization of the dehydrogenases of this organism was attempted by a study of the action of certain inhibitors and activators. The effect of *p*H and also enzyme concentration and substrate concentration were examined. *H. J. Bensted*

Chomiczewski, J. Spostrzeżenia nad dynamika typów bakteriofagowych *Salmonella typhi* w środowisku endemicznym. [**Observations on Changes in the Phage Type of *Salmonella typhi* in an Endemic Environment**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 3, 195–203. [38 refs.] English summary.

The author reports the results of the phage-typing of 1548 strains of *Salmonella typhi* isolated from patients and carriers in the absence of an epidemic in Lodz, Poland, in 1956–58. The types most frequently encountered were A (isolated from 11·93% of cases), C_1 (8·25%), E_1 (16·51%) and F_1 (23·85%). During the period under review the frequency of type E_1 declined from 21·05% in 1956 to 13·89% in 1957 and 8·33% in 1958, whereas the frequency of type F_1 rose from 9·21% in 1956 to 44·45% in 1958. *D. J. Bauer*

Williams, R. B. & Dodson, Marie W. ***Salmonella* in Alaska.** *Pub. Health Rep.* Wash. 1960, Oct., v. 75, No. 10, 913–16. [11 refs.]

SEN, R. & COLLARD, P. ***Shigella* Serotypes isolated in Ibadan, Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 574–7, 1 fig. [29 refs.]

"(1) Three hundred and two strains of shigellae were isolated from Nigerians and Europeans in Ibadan during 1956–58 and compared with those reported from some other parts of Africa.

"(2) The isolation of two serotypes *Shigella dysenteriae* 8 and *Shigella boydii* 15, which have not previously been described in Nigeria, are reported.

"(3) The possible place of infants in the epidemiology of shigella infection in Ibadan is discussed."

NOVGORODSKAYA, E. M. **Comparison of Dysentery Bacteria isolated and classified in the USSR with Cultures from Foreign Collections classified in Terms of the International Nomenclature.** *Internat. Bull. Bact. Nomencl. & Taxon.* 1960, Oct. 15, v. 10, No. 4, 239–46. [11 refs.]

Shigella serotypes recognized by Russian bacteriologists were compared with cultures of serotypes distributed by the International Shigella Centres in London and Atlanta. Most of the serotypes found in Russia have been isolated also in other parts of the world.

The commonest dysentery bacillus found in Russia is *Shigella sonnei.* *S. T. Cowan*

KALYANPUR, S. G. & WALSH, E. O'F. **Malic Acid Synthesis in *Escherichia coli* and its Inhibition by Cocaine.** [Correspondence.] *Nature.* 1960, Dec. 10, v. 188, 939–40.

GUEST, J. R. & WOODS, D. D. **Cobalamin and the Enzymic Formation of a Factor concerned in the Synthesis of Methionine by *Escherichia coli*.** *Biochem. J.* 1960, Dec., v. 77, No. 3, 422–30, 2 figs. [17 refs.]

KORNBERG, H. L., PHIZACKERLEY, P. J. R. & SADLER, J. R. **The Metabolism of C_2 Compounds in Micro-Organisms. 5. Biosynthesis of Cell Materials from Acetate in *Escherichia coli*.** *Biochem. J.* 1960, Dec., v. 77, No. 3, 438–45, 4 figs. [45 refs.]

FESSLER, Liselotte I., KELEMEN, Marianne V. & BURTON, K. **Synthesis of Protein in a Purine-Requiring *Escherichia coli* infected with Bacteriophage T2.** *Biochem. J.* 1960, Dec., v. 77, No. 3, 558–63, 4 figs. [24 refs.]

GOLDSTEIN, A. & BROWN, B. J. **Amino Acid Starvation in an *Escherichia coli* Auxotroph. III. Incorporation of ^{32}P into Ribonucleic Acid and other Cell Components.** *Biochim. et Biophys. Acta.* 1960, Nov. 18, v. 44, No. 3, 491–500, 1 fig. [18 refs.]

TAUSSIG, A. **The Synthesis of the Induced Enzyme "Cyanase", in *E. coli*.** *Biochim. et Biophys. Acta.* 1960, Nov. 18, v. 44, No. 3, 510–19, 4 figs. [10 refs.]

DRAKULIC, M., ŠMIT, S. & STAVRIC, S. **Biosynthesis of Acid-Soluble Nucleic Acid Precursors in Ultra Violet-Irradiated and Chloramphenicol-Treated *Escherichia coli B*.** *Biochim. et Biophys. Acta.* 1960, Dec. 4, v. 45, No. 1, 77–81, 4 figs.

MIDGLEY, J. E. M. **Variations in Ribulose Isomerase Activity and the Rate of Pentose Disappearance during Adaptation of *Bact. lactis aerogenes* to D-Arabinose.** *Proc. Roy. Soc.* Ser. B. 1960, Nov. 29, v. 153, No. 951, 250–62, 5 figs. [14 refs.]

SAKAZAKI, R. & NAMIOKA, S. **Serological Studies on the Cloaca *(Aerobacter)* Group of Enteric Bacteria.** *Japanese J. Med. Sci. & Biol.* 1960, Apr., v. 13, Nos. 1/2, 1–12. [14 refs.]

In a previous paper [this *Bulletin*, 1958, v. 33, 691] the authors described their method of differentiating "typical Cloaca cultures" from Klebsiella by certain biochemical tests and here report the results of their serological studies on 170 strains of the organism, now known as *Aerobacter cloacae.* By agglutination and agglutination-absorption tests they established the presence of 53 O-antigen groups and 56 H-antigens by which means they were able to recognize 79 serotypes for the Cloaca group. They found, as a general rule, that the so-called K antigen of this group was not a true capsular antigen but had the characters of a slime antigen. It would appear that a wider survey of *A. cloacae* might considerably increase the number of recognizable sero-types. *H. J. Bensted*

FISHER, M. W., PEARSON, Iris A. & MANNING, Mary C. **The Activity of Penicillin against *Proteus in vitro* and in Experimental Infections of Mice.** *Antibiotics & Chemotherapy.* New York. 1960, Oct., v. 10, No. 10, 608–11. [16 refs.]

2 strains of *Proteus vulgaris* and 2 of *Proteus mirabilis* were inhibited in broth by concentrations of penicillin varying from 3·1 to 12·5 μgm./ml. Mice given a lethal intraperitoneal inoculum of these organisms were saved by a single moderate dose of penicillin (CD50 = 35–84 mgm./kgm.) given subcutaneously at the time of inoculation, but only by larger doses given 4 hours later. It is thus wrong simply to describe this genus as resistant to penicillin, which may indeed have some place in treating infections due to these organisms. *L. P. Garrod*

BACHRACH, U. **A Simple and Rapid Technique for the Identification of Proteus-Providence Strains.** *J. Clin. Path.* 1960, Nov., v. 13, No. 6, 525–6. [10 refs.]

GARGANI, G. La titolazione degli antigeni brucellari mediante la reazione di fissazione del complemento ed una proposta di modificazione al modello della costituzione antigene del genere "*Brucella*". [**Titration of *Brucella* Antigen by means of Complement-Fixation Reaction and a Proposal to modify the Pattern of Antigenic Constitution of the Genus "*Brucella*"**] *Ann. Sclavo.* Siena. 1960, July–Aug., v. 2, No. 4, 383–96, 1 diagram. [13 refs.] English summary.

Extensive observations on the complement-fixing titres of the sera of rabbits injected with *Brucella abortus*, *Brucella melitensis* and *Brucella suis* respectively are presented. They were tested with antigens prepared from these bacteria, which were limpid supernatants spun out from the bacterial detritus after repeated thawing and freezing. The rises in titre between the fifth and seventh days after infection are usually striking.

A greater antigenic resemblance was found between the *melitensis* and *suis* strains which diverged considerably from the *abortus* strains, although cross-reactions appeared between all three. It is claimed that each of these bacteria contain A, M and Su antigen, A being maximal in *abortus* and slight in the other two, M. maximal in *Melitensis* but considerable in the two others, Su maximal in *suis*, considerable in *melitensis* and slight in *abortus*. [The experimental results scarcely justify these last conclusions.]

J. W. McLeod

PARNAS, J., with the collaboration of Jadwiga POJASEK & DANUTA-GIERIATOWICZ. Études nouvelles sur la réaction opsono-phagocytaire au cours de la brucellose. [**Studies on the Opsono-phagocytic Reaction During *Brucella* Infections**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 550–65, 7 figs. [13 refs.]

This paper compares the results of the original opsono-phagocytic reaction of HUDDLESON with the modification which employs inactivated serum, with the avirulent brucella strain S19 and also a virulent brucella strain.

It was found that the original method of Huddleson gave the best results with guineapigs immunized with strain S19 and samples examined 4 weeks after vaccination. The counting of 50 leucocytes for the phagocytic index is recommended and the use of the avirulent strain was found to give better results for the actual test than the virulent strain. The use of rough strains or sensitized strains should not be used for the estimation of the opsono-phagocytic index as their activity is non-specific.

H. J. Bensted

PARNAS, J. & DANUTA-GIERIATOWICZ. Recherches nouvelles sur l'influence de l'A.C.T.H. sur les phénomènes immunologiques au cours de la brucellose. [**Studies on the Influence of Corticotrophin on Immunological Reactions During *Brucella* Infections**] *Rev. d'Immunologie.* 1960, July-Sept., v. 24, No. 4, 566–74, 3 figs.

Previous experience by the author on the effect of ACTH [corticotrophin] on animals infected with the avirulent strain of *Brucella*, S19, had failed to show any significant change in their immunity reactions. In the present paper he describes the effect of ACTH on guineapigs administered before they were infected with a virulent strain of *Brucella*. It was found that the development of agglutinins, complement-fixing antibody and the opsono-phagocytic reaction was delayed and the levels were lower in the test animals than in the controls but that the intradermal sensitivity reaction was enhanced.

[In describing the experiments it is indicated that both guineapigs and rabbits were used for the tests but the results reported refer only to the guineapig tests. SHEWELL and LONG [this *Bulletin*, 1957, v. 32, 295] showed that whereas the rabbit was cortisone-sensitive the guineapig, like man, was resistant in that its antibody-forming capacity was unaffected by cortisone.] *H. J. Bensted*

MATHUR, T. N. **The Development of *Brucella* Agglutinins in Cholera inoculated Persons.** *Indian J. Med. Res.* 1960, May, v. 48, No. 3, 309–14.

This paper reports the examination of the sera of 174 Indian subjects for *Brucella* agglutinins after the inoculation of cholera vaccine. The period between the cholera inoculations and the serological examinations varied from 4 days to 5 months and 121 subjects had received a single dose of cholera vaccine and 53 had had 2 doses with an interval of 7 days. In most cases where two doses were given it appears that the sera were examined before inoculation and once after, but some had a third serum examination at a later date although the actual number is not always obvious. The great majority of the persons who received only a single dose of vaccine are not shown to have had their pre-inoculation serum examined. The author reports that after one dose of cholera vaccine 42% showed brucella agglutinins and after 2 doses the figure was 45%, but in both groups the agglutinin level was low and this tended to fall to even lower levels after a period of 4–5 months while the cholera agglutinin levels will be much higher.

The sera of 20 patients suffering from active brucellosis were also examined and 5 of these, apparently not inoculated against cholera, had low titre agglutinins to *Vibrio cholerae*.

The work reported in this paper was not fully controlled and its significance is uncertain but it will be recalled that EISELE *et al.* [this *Bulletin*, 1948, v. 23, 179] drew attention to the development of brucella agglutinins after cholera vaccination and that MCCULLOUGH *et al.* [*ibid.*, 898] and GALLUT [*Trop. Dis. Bull.*, 1951, v. 48, 255] claimed that *V. cholerae* and *Brucella* shared a minor antigen. *H. J. Bensted*

KNOX, K. W. & BAIN, R. V. S. **The Antigens of *Pasteurella multocida* Type I. I. Capsular Polysaccharides.** *Immunology.* Oxford. 1960, Oct., v. 3, No. 4, 352–62. [25 refs.]

SOLTYS, M. A. **A New Method of demonstrating Capsulated *Bacillus anthracis*.** *J. Clin. Path.* 1960, Nov., v. 13, No. 6, 526–7.

BARBER, Cella, PETROVICI, A., ZILIŞTEANU, Eugenia & NAFTA, I. Recherches sur les haptènes du bacille *anthracis* et leur localisation dans le cellule bactérienne. [**Investigations concerning the Haptens of the Anthrax *Bacillus* and their Localization in the Bacterial Cell**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Sept., v. 19, No. 3, 379–89, 3 figs. & 3 pls. [14 refs.]

PURKAYASTHA, M. & NANDI, P. **Antibiotic Substances from a Strain of *Bacillus subtilis*.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 114–19.

PRZYBOROWSKI, R., HORN, H. & HERTWIG, F. Beitrag zur Kenntnis der aeroben Bazillen der Mesentericus-Subtilis-Gruppe. [**Observations on Aerobic Bacilli of the Mesentericus-Subtilis Group**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Oct., v. 6, No. 10, 659–75, 11 figs. [31 refs.]

KATITCH, R. V. Résultats de nos recherches sur le problème de la bactériémie du tétanos. [**Observations on the Question of Bacteriaemia in Tetanus**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 525–9.

The observations were entirely experimental and dealt with the penetration of the bacteria into the lymphatic glands and the penetration of the intestinal wall by toxin as a sequel to injection of tetanus bacilli. Tetanus bacilli were not grown from the lymphatic glands as a sequel to injection of culture to the muscles in a normal animal, but they did appear in the lymphatic glands if the reticulo-endothelial system was blocked by injections of Congo red to the thigh muscles and removal of the spleen before the injection of the tetanus bacilli. Mice which ingested cultures of *Clostridium tetani* developed intoxication if, at the same time, bile or powdered glass was given to produce an intestinal lesion. The previous oral administration of toxigenic culture of *Escherichia coli* did not facilitate the development of tetanus intoxication in the same way.

[The experimental evidence and the conclusions are rather slender.] *J. W. McLeod*

D'ARCA SIMONETTI, A. Sulla specificità della reazione per la ricerca *in vitro* della tossinogenesi dei germi anaerobi. [**Specificity of "*in vitro*" Observations on Toxigenesis by Anaerobes**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Mar.–Apr., v. 11, No. 2, 105–14, 1 fig. [12 refs.] English summary.

In these observations liver extract agar, or in cases of difficulty agar in which the ingredients of Bacto Brewer thioglycollate medium were incorporated, was inoculated with the anaerobe under investigation.

The inoculated agar was then poured to a plate and a sterile coverslip used to cover part of the surface before the medium had set completely, as in the technique of V. DEL VECCHIO [this *Bulletin*, 1955, v. 30, 443]. As soon as an adequate but not excessive growth of the anaerobe had occurred beneath the coverslip a few drops of the specific antiserum were introduced to a cup in the vicinity and after a further 24 hours of incubation the plate was kept at room temperature and observed for the appearance of lines of precipitation for 10 days or longer if the condition of the culture remained satisfactory.

A wide range of anaerobes from the collection of the Istituto Superiore di Santà, and *Cl. botulinum* strains A, B, C, D and E obtained from Dr. A. R. PRÉVOT of Paris, were examined. They were tested with the antitetanic serum of the Istituto Sieroterapico of Milan and with anti-*welchii, sordellii, oedematiens* and 5 type-specific anti-*botulinum* sera from Paris. The chief findings were crossed reactions between anti-*botulinum* sera A and B and the corresponding bacteria, and also between antisera C and D and these bacteria. *Cl. botulinum* E never reacted positively with any other than E antiserum, but that antiserum gave lines of precipitation with strains A and B. *J. W. McLeod*

ERRATUM

The Editor regrets that in the abstract of the paper by SHIRVINSKAIA, this *Bulletin*, 1961, v. 36, 85, the first and the last lines of the second paragraph were incorrect. This paragraph should read:

" The author studied the protective properties of hyperimmune rabbit sera (titres 11,000–20,000) prepared from strains of the following serotypes of *Leptospira*: *icterohaemorrhagiae* AB, *canicola, poi, bataviae, saxkoebing, hebdomadis, grippotyphosa, pomona*, and *hyos*. Before being used in the experiments, the virulence of these strains was enhanced by 5–8 serial passages in animals [presumably young rabbits] until typical symptoms, and death in 75–90%, resulted. *L. icterohaemorrhagiae* A (Kantarowicz strain) was avirulent and could only be used for production of immune serum."

KEELER, R. F. & GRAY, M. L. **Antigenic and Related Biochemical Properties of *Listeria monocytogenes*. I. Preparation and Composition of Cell Wall Material.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 683–92, 4 figs. [34 refs.]

BACTERIOPHAGES

ROBINSON, J. B., DOUGLAS, R. J., GRINYER, I. & GARRARD, E. H. **Chromatography of Coliphages T_1 and T_2 on Columns of Calcium Phosphate.** *Canadian J. Microbiol.* Ottawa. 1960, Oct., v. 6, No. 5, 565–72, 8 figs. (1 on pl.) [11 refs.]

Phages T1 and T2 have been purified by adsorption to columns of calcium phosphate (brushite) and elution by increasing concentrations of phosphate buffer at *p*H 6·8. A small column with a retention volume of 2 ml. could adsorb 2×10^{12} plaque forming units of T2, and phage was easily concentrated 10-fold. Neither T1 nor T2 adsorbed unless the lysates were first dialysed against water. About 12% of a T2 lysate was eluted by 0·03 M and about 68% by 0·2 M buffer. The 2 fractions were serologically identical and their separation was in fact due to a chromatographic artefact, probably a "displacement effect" happening when elution of other constituents of the lysate carried some phage down too. When each fraction was dialysed and rechromatographed separately, each was eluted by 0·2 M buffer, but when the fraction recovered in 0·2 M buffer was put down a column which had been pre-treated with dialysed broth, phage was eluted in 2 fractions, about 8% coming off in 0·03 M and the rest in 0·2 M buffer.

T1 phage was also eluted in 2 fractions, about 5% coming off in 0·04 M and 55% in 0·06 M buffer. Unlike the findings with T2 however, non-phage material in the lysate was not responsible for this fractionation as each fraction, after dialysis and rechromatography, was again eluted by the same concentration of buffer as before.

Since T1 and T2 were eluted by different concentrations of buffer, mixtures of the phages could be separated by chromatography. Protein estimations done on the eluted material showed that considerable purification had been achieved. However, electron micrographs of T2 purified by 2 cycles of adsorption and elution showed that many small electron-dense particles were still present in the phage suspension. *Janice Taverne*

CUMMINGS, D. J. & KOZLOFF, L. M. **Biophysical Properties of Bacteriophage T2.** *Biochim. et Biophys. Acta.* 1960, Nov. 18, v. 44, No. 3, 445–58, 4 figs. [24 refs.]

"Biophysical properties of bacteriophage T2 and T2 'ghosts' have been studied using the ultracentrifuge, the electron microscope and the diffusion apparatus. The molecular weight of T2 at either pH 7 or pH 5 has been found to be $215 \cdot 10^6$. The protein portion of the head of the intact particles or of the DNA-free phage ghost has been found to exist in two forms, depending on both pH and temperature. One head form of intact T2 is approximately 15% longer than the other; 119 mμ by 80 mμ *vs.* 103×80 mμ. Raising either the temperature or the pH favors the formation of the longer head form. This change in head form accounts for the dual sedimentation phenomenon observed now for T2 ghosts and reported previously for intact T2. Estimates have been made of the thermodynamic changes involved in the transition of one form to the other."

YOUNG, B. G. & MORA, P. T. **Viability of T2 Bacteriophage after Interaction with Negatively Charged Macromolecules.** *Virology.* New York. 1960, Nov., v. 12, No. 3, 493–5, 1 fig.

KUBINSKI, H. **Studies on the Mechanism of the Reaction between Phage *T2* and the Eluate from *Escherichia coli* B.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 9, 383–8, 3 figs.

"The investigations concerned the mechanism involved in sensitization to potassium permanganate of phage *T2* by extracts from *Escherichia coli* B. Changes in the sensitizing factor's activity were found to result from its decomposition, to which an enzymatic nature is ascribed. The observations made implicated an enzyme of the phage particle itself."

KUBINSKI, H. **Further Investigations on the Reaction between Phage *T2* and Substances from *Escherichia coli* B Cells.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 9, 389–93, 2 figs. [23 refs.]

"It has been established in this paper that substances contained in the native eluate obtained from *Escherichia coli* B cells react with bacteriophage *T2* changing the kinetics of its adsorption to host cells and increase its susceptibility to temperature. The observed phenomena are discussed."

GOODMAN, F.; SAUKKONEN, J. J.; CHARGAFF, E. **Patterns of Cellular Controls operating in Bacteriophage Reproduction. I. Effect of 5–Fluorouracil on the Multiplication of Several Coliphages** [GOODMAN, SAUKKONEN & CHARGAFF]. *Biochim. et Biophys. Acta.* 1960, Nov. 18, v. 44, No. 3, 458–68, 4 figs. [19 refs.] **II. Effect of 5–Fluorouracil on Metabolic Events in Bacteria infected with Coliphage T2r+** [SAUKKONEN, GOODMAN & CHARGAFF]. *Ibid.*, 469–77, 1 fig. [20 refs.]

STREISINGER, G. & BRUCE, V. **Linkage of Genetic Markers in Phages T2 and T4.** *Genetics.* 1960, Sept., v. 45, No. 9, 1289–96, 4 figs. [10 refs.]

"This report describes sensitive tests of linkage which have indicated that all the known markers of the T-even phages can be arranged in one linkage group. The results presented here agree with the independent findings of BAYLOR *et al.* (1957), who found a marker linked to both of previously unlinked groups in T2, and with those of MCFALL and STENT (1958), who described a genetic anomaly affecting markers on each of the remaining two groups, thus linking them."

TANAMI, Y. **Some New Host-Range Phenotypes of T4D Bacteriophage and their Genetic Control.** *Virology.* New York. 1960, Nov. v. 12, No. 3, 422–30, 1 fig. [21 refs.]

LEHMAN, I. R. & PRATT, E. A. **On the Structure of the Glucosylated Hydroxymethylcytosine Nucleotides of Coliphages T2, T4, and T6.** *J. Biol. Chem.* 1960, Nov., v. 235, No. 11, 3254–9, 7 figs. [24 refs.]

TESSMAN, Ethel S. & OZAKI, T. **The Interaction of Phage S13 with Ultraviolet-Irradiated Host Cells and Properties of the Ultraviolet-Irradiated Phage.** *Virology.* New York. 1960, Nov., v. 12, No. 3, 431–49, 7 figs. [29 refs.]

"Phage S13 shows most of the interactions with ultraviolet (UV)-irradiated host cells that are typical of temperate phages and their virulent mutants. The UV sensitivity of capacity of *Escherichia coli* C to reproduce unirradiated S13 is of the same order of magnitude as the UV sensitivity of colony-forming ability and is much greater than the UV sensitivity of T3 capacity. Capacity is partially restored by multiple infection with S13, a finding that supports the hypothesis of obligatory pairing between phage and host genomes. The radiosensitivity of capacity for UV-irradiated S13, T1, and T3 and for normal S13 are all approximately the same. This result implies that the reactivation of UV-irradiated T1 and T3 by the cell may occur by the same interaction between phage and host genomes that normally occurs in the reproduction of S13. The dose on the cells for maximum UV-reactivation (UVR) is the same for S13 with *E. coli* C, T3 with B or B/r, and T1 with B/r. A large increase in the frequency of plaque-type mutants accompanies UVR for S13. A small amount of cross reactivation of a host range marker was detected for S13, but no multiplicity reactivation of the phage was detected either with normal or UV-irradiated cells."

LURIA, S. E., ADAMS, J. N. & TING, R. C. **Transduction of Lactose-Utilizing Ability among Strains of *E. coli* and *S. dysenteriae* and the Properties of the Transducing Phage Particles.** *Virology.* New York. 1960, Nov. v. 12, No. 3, 348–90, 6 figs. [Numerous refs.]

"Transduction of the *lac*$^+$ property by phage P1 among strains of *Escherichia coli* K12 and *Shigella dysenteriae* Sh has been studied. When *E. coli* strains are used both as donors and recipients, transduction gives stable *lac*$^+$ transductants (transduction by integration). Transduction from *E. coli lac*$^+$ donors to strain Sh gives mainly unstable, *lac*^{v} transductants, in which the *lac*$^+$ genes are apparently associated with some phage P1 genes in a defective prophage, called P1 *dl* (transduction by lysogenization). A variety of P1 *dl* elements is postulated to account for the properties of different Sh *lac*^{v} transductant strains. Some of these strains produce phage lysates that transduce the *lac*$^+$ property at high frequency (HFT lysates), probably because of a high content of phage particles carrying the defective phage element P1 *dl*. A different type of P1 *dl* element called P1 dl_w has been obtained by using HFT lysates from Sh *lac*^{v} strains to transduce the *lac*$^+$ property in a strain of *E. coli* that appears to have a deletion of the *lac* genetic region.

"The results of *lac*$^+$ transduction by various types of lysates to various recipient strains have been compared, using both untreated and ultraviolet-irradiated lysates. The results are interpreted by assuming that the transducing particles contain genetic elements with various combinations of phage genes and of bacterial genes, and that the transduction type that is obtained, by integration or by lysogenization, depends both on the ability of the transducing elements to lysogenize and on the degree of genetic homology between the donor and the recipient of the transduced bacterial genes. High genetic homology favors integration; low genetic homology hinders integration and allows detection of transductants carrying the transducing element as prophage."

MOSELEY, B. E. B. & GORRILL, R. H. **An Effect of Early Dilution on the Establishment of Lysogeny in *Salmonella typhimurium*.** [Correspondence.] *Nature.* 1960, Nov. 26, v. 188, 755, 2 figs.

When *Salmonella typhi-murium* LT2 was infected with phage P22 and samples were removed at intervals and diluted into broth or buffer at room temperature or at 37°C., the percentage of cells becoming lysogenic increased to reach a maximum at 6 minutes then fell to a minimum at 12 minutes. If the infected complexes were left without being diluted, only 20% became lysogenic, the rest being lysed. If they were diluted between 4 and 8 minutes after infection, over 80% became lysogenic and only 20% gave the lytic response.

LWOFF *et al.* [this *Bulletin*, 1954, v. 29, 860] showed that the "decision" period, the time when *Salm. typhimurium* infected with Al phage made the decision to lyse or to become lysogenic, occurred 6–10 minutes after infection. When chloramphenicol is present during this period, cells which would otherwise lyse become lysogenic, [BERTANI, *ibid.*, 1957, v. 32, 1186]. These results show that dilution of infected *Salm. typhi-murium* LT2 cells into fresh medium before the decision to lyse is made also results in the establishment of lysogeny by phage P22. *Janice Taverne*

BRINLEY-MORGAN, W. J., KAY, D. & BRADLEY, D. E. ***Brucella* Bacteriophage.** [Correspondence.] *Nature.* 1960, Oct. 1, v. 188, 74–5, 2 figs.

There have been several papers published recently on the bacteriophages of *Brucella* [PARNAS; VAN DRIMMELEN; Lois JONES; REDFEARN and BERMAN; Madame DROZHEVKINA and others, this *Bulletin*, 1958, v. 33, 1180; 1959, v. 34, 282 *bis*, 334, 392, 439, 582, 684, 1053; 1960, v. 35, 157, 304, 1239 *ter*; 1961, v. 36, 82, 298]. Most of the work recorded in these papers stems from the original observations made on the "Tbilisi" phage isolated in the U.S.S.R. from manure. Although other phages have since been isolated and some show certain differences in patterning their host range has in the main been restricted to typical strains of *Brucella abortus*. In the paper by Lois

Jones [*ibid.*, 1960, v. 35, 1239] attention was drawn to a personal communication which the author had received from STABLEFORTH and BRINDLEY-MORGAN concerning a phage sent by Parnas to Weybridge. The Weybridge workers had found that this phage was not only active against typical *Br. abortus* strains but also against certain strains of *Br. Melitensis* isolated from cattle in England.

The first part of the present paper is concerned with the observations already recorded by Lois Jones. The second part is concerned with the morphology of this particular phage strain sent through WHO to Weybridge. The original description gave the diameter of the phage as 60–80 mμ. and stated that it possessed no tail, whereas the present authors find that the phage particles, by electron microscopy, has a diameter of 65 mμ. and bears a wedge-shaped tail, 14 mμ. long attached to one corner. The morphology of this phage is said to be indistinguishable from the coli phage T3. *H. J. Bensted*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

LENAHAN, Margaret F. & WENNER, H. A. **Propagation of Entero- and Other Viruses in Renal Cells obtained from Non-Primate Hosts.** *J. Infect. Dis.* 1960, Sept.-Oct., v. 107, No. 2, 203–12, 3 figs. [26 refs.]

The spectrum of growth of viruses in a variety of kidney cells is reported. Calf, lamb, pig, hamster, dog, cat, rabbit and mouse cells were compared with each other and human amnion and monkey kidney cells. The paper must be consulted for the individual details. It was found that calf, lamb, pig and hamster kidney cells were susceptible to many ECHO, Coxsackie B, adeno and other viruses. Dog, cat, rabbit and mouse kidney cells had a narrower spectrum. In fact, the host range of different viruses could be used as a method of identification, although the authors point out that results obtained with strains of virus studied by them differed from reports in the literature. *A. J. Beale*

POLLOCK, M. E., KENNY, G. E. & SYVERTON, J. T. **Isolation and Elimination of Pleuropneumonia-Like Organisms from Mammalian Cell Cultures.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 10–15, 1 fig. [19 refs.]

Many cell lines have been found to be contaminated with pleuropneumonia-like organisms (PPLO). The authors have investigated 166 cell lines or sublines and found 57% contaminated. The best method for detection was to add freshly trypsinized cells to a special broth medium (pancreatic digest of beef heart as described by BROWN (*J. Bacteriology*, 1948, v. 55, 871) and ROBINSON *et al.*, [this *Bulletin*, 1952, v. 27, 693]. The broth cultures were subsequently inoculated on to sloppy agar. It was found that kanamycin treatment cured the PPLO infection. The duration of treatment required was inversely proportional to the dose of kanamycin. Thus, 1,000 μgm. per ml. cured cells in 1 hour whereas 10 hours were required with 100 μgm. per ml. The standard treatment employed was 100 μgm. per ml. for 3 weeks although 48 hours was probably more than adequate. After treatment cells were maintained in antibiotic-free medium. The cell lines were maintained in a variety of media with many different types of sera. After treatment cells remained free of PPLO. In view of this it seems unlikely that the serum used is the source of PPLO. The organisms could be L forms of bacteria induced by antibiotics often used in cell growth medium. They could also be human PPLO derived from tissue culturists. It seems, however, that whichever is the true source, the problem can be overcome by rigid aseptic precautions. *A. J. Beale*

TOVARNITSKII, V. I. & TIKHONENKO, T. I. **The Infective Properties of Viral Nucleic Acids.** *Russian Rev. Biol.* London. 1960, June, v. 49, No. 1, 15–30. [Numerous refs.] [Translated from Russian *Uspekhi Sovremennoi Biol.*]

ANN. NEW YORK ACAD. SCI. 1960, Jan. 13, v. 83, Art 4, 513–760, numerous figs. [Numerous refs.] **Inactivation of Viruses** [POLLARD, E. C. & TAYLOR, A. R. (Conference Co-Chairmen)]. [Conference held Mar. 19 and 20, 1959.]

In March 1959 the New York Academy of Sciences held a 2-day symposium on inactivation of viruses and have now published the main papers in full. The first session was devoted to biological inactivation of viruses. B. MANDEL (pp. 515–527) gave an account of his studies of the serum neutralization reaction with the use of poliovirus and plaque counting for detecting residual virus. The complexity of the factors involved is stressed but the means for their elucidation are now to hand. Virus inactivation follows first order kinetics in excess antibody but there is a persistent residual fraction of unneutralizable virus. The nature of this fraction is unknown. In the poliovirus system virus does not dissociate from antibody appreciably at *p*H 7·2 but does completely at *p*H 2·5.

Three papers were given on non-specific serum inactivation of viruses with special reference to the properdin system. This is a complex subject not made a great deal clearer, although N. S. GINSBERG and R. J. WEDGWOOD (528–532) provide a useful short review. R. W. SPEIR and C. M. SOUTHAM (pp. 551–563) describe experiments in which the neuropathogenicity of Egypt 101, Mengo or Bunyamwera viruses was interfered with to some degree by the prior administration of Newcastle disease virus. Mice bearing Ehrlich ascites cell tumours lived longer if infected with Bunyamwera virus and the palliative effect was enhanced if NDV was also administered.

During the second session, on chemical inactivation of viruses, there was a series of papers on the inactivation of poliovirus by formaldehyde by S. GARD (pp. 638–648), J. E. SALK and B. GORI (pp. 609–637), F. L. SCHAFFER (pp. 564–577), J. CHARNEY, W. P. M. FISCHER, J. F. SAGIN and A. A. TYTELL (pp. 649–653) and, in discussion, by I. W. MCLEAN (pp. 753–760). On the one hand Salk, supported by studies on purified high titre virus by Charney [and also in the discussion, not reprinted, by BAZELEY], showed results compatible with inactivation following first order kinetics. Factors causing a departure from a straight line inactivation are: heterogeneity of virus particles, *e.g.* viral aggregates due to inadequate filtration; low temperature inactivation; storage conditions, thus a proportion of the particles in freshly harvested virus is relatively unstable and undergoes more rapid inactivation as first demonstrated by TIMM *et al.*, [this *Bulletin*, 1957, v. 32, 1007]. Linear inactivation occurs thereafter. Gard, on the other hand, stressed the complexities. Virus suspensions, even when pure, consist of a nucleic acid core surrounded by a protein coat and it is to be expected, therefore, that the reaction will occur in stages. Schaffer, in studies on purified poliovirus, found that inactivation by formaldehyde at 37°C. was not linear but fitted closely the empirical formula given by Gard. McLean, too, stressed the complexities and presented an inactivation curve which was not linear. O. N. FELLOWES (595–608), in a long and discursive paper, touched on the complexities involved in preparing foot and mouth disease vaccines. G. A. LOGRIPPO (578–594) stressed the merits of β propiolactone for sterilization and viral inactivation with particular reference to treating blood products to reduce the hazards from hepatitis. It is important to use the pure substance and preferably to combine it with ultraviolet inactivation. The effect of β propiolactone on viruses, *e.g.* T3 bacteriophage, poliovirus and eastern equine encephalitis, is illustrated. Lastly, the non-toxicity of β propiolactone is stressed.

8 papers were given on physical means of virus inactivation in the third session. E. C. POLLARD, in an introductory survey of the methods available (pp. 654–660), felt that physical as opposed to chemical means of inactivation were insufficiently studied. They should in future yield important theoretical advances and be of value for the preparation of vaccines. A. KLECZKOWSKI (pp. 661–669) presented a paper on ultraviolet inactivation of plant viruses with a criticism of the single hit theory of inactivation. A. R. TAYLOR (670–683) presented an account of ultraviolet inactivation of animal viruses, in particular the development of the Centrifilmer unit for producing thin stable films for inactivation and its application to poliovirus vaccine manufacture. C. R. FUERST (pp. 684–691) gave a short review illustrating the power of radiobiological inactivation methods in the study of bacteriophage and suggested that these techniques could be applied with profit to the problem of animal viruses. J. F. MCCREA (pp. 692–705) reviewed work on ionizing radiations stemming from the classical studies of LEA and SALAMAN [*ibid.*, 1942, v. 17, 511; *Action of Radiations on Living Cells*, New York, 1947, Cambridge University Press]. He presented new work on the inactivation of vaccinia virus suggesting that the sensitive target diameter for infectivity was 46 to 50 millimicrons and for haemagglutinin 9 millimicrons. He shows that for animal viruses larger than 45 mμ the radiosensitive infectious unit is remarkably constant at 40 to 58 mμ regardless of the exact physical size of the intact particle. G. T. DIMOPOULLOS (pp. 706–726) gave a long and involved paper about the survival of foot and mouth disease virus. This paper was not technically very good. N. A. LAUFFER (pp. 727–740), in a very interesting paper on tobacco mosaic virus, discusses the effect of physical methods of inactivation on the intact virus and on the infectious nucleic acid derived from it. The effect of these agents is largely on the nucleic acid component. C. WOESE (pp. 741–751) presented a *tour de force*, blinding the biologists with mathematical brilliance. He postulates that thermal inactivation of viruses is an effect on the nucleic acid; that this nucleic acid occurs in 2 forms—a stable form B and a less stable form A. Two kinds of inactivation, a mass breaking of hydrogen bonds giving collapse of the secondary structure and a breaking of the nucleic acid chains, can occur. It is supposed that chain breaking occurs at lower temperatures and that antigenic structure is not altered. Therefore, inactivated vaccines could be made by low temperature inactivation. He goes on to suggest that formaldehyde inactivation is really primarily thermal inactivation. This paper has a wealth of mathematical argument and leaves a biologist amazed. *A. J. Beale*

HALLUM, J. V. & YOUNGNER, J. S. **The Effect of Oxidative Controlled Potential Electrolysis on Viruses.** Virology. New York. 1960, Oct., v. 12, No. 2, 283–308, 11 figs. [16 refs.]

"A method is described for inactivation of viruses by oxidation at controlled potentials. If the applied potential is adjusted properly, it is possible to destroy the infectivity of the viruses without changing other properties. The rate of loss of infectivity is shown to be dependent upon the applied potential and the purity of the virus preparation used. Control experiments are described which indicate that the loss of infectivity is due to oxidation of the viruses at the surface of the working electrode. Contact of the viruses with this electrode is necessary for the inactivation to occur.

"A method is also described which relates the 'resting potential' of the electrolytic cell to the number of electrons transferred per functional group on the virus particle."

NEUSTROEV, V. D. & MILIUTIN, V. N. **An Experimental Study of Ornithosis Virus in Various Stages of Development.** *Problems of Virology.* London. 1959, v. 4, No. 5, 95–102, 4 figs. [17 refs.] [Translated from Russian.]

The authors report their findings in a study of the development of the agent of ornithosis in the brain and lung of inoculated mice, in the yolk sac of chick embryos and in HeLa cell cultures. Morphological changes were followed by fluorescence microscopy with acridine orange staining, and these changes were correlated with virulence and toxicity by means of viral counts and titrations in mice.

[Judging by the illustrations fluorescence microscopy, as used by the authors, would not seem in any way superior to ordinary microscopy for the study of the developmental forms of this agent. And their findings add nothing to previous work by others. The confirmation of the observation of HURST *et al.*, [this *Bulletin*, 1951, v. 26, 442] that penicillin gives rise to giant large ("vegetative") forms is interesting. Reference is not made to this earlier work, nor is it pointed out that penicillin can produce giant forms from susceptible bacteria as the result, it is believed, of interference with division.] *S. P. Bedson*

NEUSTROEV, V. D., KHANDUEV, Z. Z. & MILIUTIN, V. N. **The Counting of the Elementary Bodies of Ornithosis Virus by Fluorescence Microscopy.** *Problems of Virology.* London. 1959, v. 4, No. 6, 106–9, 1 fig. [Translated from Russian.]

Unit volumes of the unknown virus suspension and a suspension of bacteria—or chick red cells—previously counted, were mixed and comparative counts made of virus particles and bacteria—or red cells—in smear preparations of the mixture. The immersion system of the fluorescence microscope and acridine orange staining were used for the purpose of counting. Comparison of the counts so obtained with virus titrations made in mice inoculated by the cerebral route, showed a variation of 10 to 67 virus particles per LD50. *S. P. Bedson*

AVAKIAN, A. A. & GAO-TIAN-'SIAN'. **Electron Microscope Studies of the Internal Structure of *Lymphogranuloma venereum* Virus in Ultrathin Section.** *Problems of Virology.* London. 1959, v. 4, No. 5, 89–95, 5 figs. [Translated from Russian.]

This paper reports on the electron microscopy of lesions produced in the lungs of mice by lymphogranuloma venereum virus administered intranasally. The affected alveolar cells showed vacuolation, absence of mitochondria and presence of cytoplasmic inclusions in the neighbourhood of the nucleus. These inclusions possessed a finely granular basic substance in which were embedded virus particles varying in size from 400 to 1,000 mμ and arranged singly, in pairs and in short chains. The fully developed virus particle consisted of a membrane surrounding a mass of viroplasm and a dense centrally-placed nucleoid; considerable pleomorphism in size and structure was, however, exhibited by the virus particles. [No mention is made of any developmental sequence in the various virus forms observed. And if the illustrations of this paper are an indication of the standard of electron microscopy used in this study, one wonders if the conclusions drawn are of value.] *S. P. Bedson*

CAIRNS, J. **The Initiation of Vaccinia Infection.** *Virology.* New York. 1960, July, v. 11, No. 3, 603–23, 10 figs. [23 refs.]

The work reported here shows, by an elegant combination of fluorescence microscopy and autoradiography, that in cells infected with vaccinia virus the number of centres where the synthesis of virus protein and deoxyribonucleic acid (DNA) takes place is proportional to the multiplicity of infection. There was, in these experiments, a lag phase (the *preparatory period*), of about 3½ hours before virus DNA and protein synthesis was detectable. It is suggested that in a cell infected by several virus particles, one of them acts as an *initiator* which accomplishes some critical step in the infective process. The greater the number of particles per cell the greater the likelihood that one will act as initiator. When synthesis does start, it does so simultaneously in each infected centre in the cytoplasm of a cell. As synthesis progresses, the centres enlarge, and those in any given cell may fuse. Up to the 10th hour the newly synthesized DNA is susceptible to the action of deoxyribonuclease. When infection spreads to neighbouring cells it is associated with spread of DNA from the originally infected cell to the neighbours. Up to the 9th hour after infection, infected cells were able to continue synthesizing their own nuclear DNA. *Colin Kaplan*

SZÁNTÓ, J. **Stable Cell Strains from Rabbit and Rat Lung Tissue, Suitable for the Propagation of Herpes Simplex Virus.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 380–82, 4 figs. on 2 pls.

POLLEY, J. R. **Preparation of a Stable Non-Infective Complement-Fixing Antigen for Herpes Simplex.** *Canadian J. Microbiol.* Ottawa. 1960, Oct., v. 6, No. 5, 515–18.

Herpes simplex complement-fixing (CF) antigen, prepared by macerating infected chick chorioallantoic membranes in saline and centrifuging to remove gross particles, was allowed to stand at 4°C. for 4 days and then centrifuged at 9,000 *g* for 1 hour. This speed had been found to remove most of the non-specific CF antigens without substantially reducing the amount of herpes CF antigen.

Experiments on inactivation with formaldehyde showed that uninfective CF antigens of highest titre were obtained either by using low concentrations of formaldehyde at 37°C. for a short time or higher concentrations at 4°C. for longer. Antigenicity was best preserved at high *p*H rather than the low *p*H which is optimum for

influenza virus. The method finally adopted was to treat with 0·01% formaldehyde at 37°C. for 2 days at *p*H 8·5 and to neutralize excess formalin with 30% dibasic ammonium phosphate. The antigen thus obtained withstood freeze drying and was stored for 1 year at 4°C. without loss of potency. *Janice Taverne*

GISPEN, R. & SAATHOF, B. **Isolation and Antigen Production of Herpes Simplex Virus in the Chorioallantoic Membrane of Duck Embryos.** *Antonie van Leeuwenhoek: J. Microbiol & Serol.* 1960, v. 26, No. 3, 241–9.

Material from skin lesions from cases of herpes simplex infection was inoculated on to the chorioallantoic membranes (CAM) of chick and duck embryos, into tissue cultures of monkey kidney cells and a line of human kidney cells, and into suckling mice intracerebrally. The highest isolation rate was obtained in suckling mice and duck eggs. 10 strains were isolated in duck eggs which never grew in hen eggs.

Duck eggs had many advantages over hen eggs in the isolation of herpes. Not only were they twice as sensitive but the virus grew to higher titres. The focal lesions were bigger, reaching a maximum after 5 days, and intranuclear inclusions in the cells were more numerous. On average, complement-fixing antigen prepared from suspensions of infected CAM had 10 times the activity of that from chick CAM. The virus was adapted more quickly to duck CAM, though once it was adapted to eggs at all it gave the same titre in duck as in chick CAM. *Janice Taverne*

SAWICKI, L. & GRZELAKOWA, Hanna. Wirus grypy w hodowli tkankowej małpiej nerki. Badania przy pomocy odczynu hemadsorpcji. [**The Growth of Influenza Virus in Monkey Kidney Tissue Culture Investigated with the Hemadsorption Technique**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 3, 241–9, 5 figs. (4 on 2 pls.). English summary.

By means of the haemadsorption test it could be shown that strains of type A (PR8), A-prime (Pan and A56), A 2 (Singapore) and B (Lee) influenza virus would multiply readily in cultures of monkey kidney tissue, attaining titres of $10^{3.5}$–10^{5}. During an epidemic of type A 2 influenza in spring 1959 in Poland 10 strains of influenza virus were isolated from material from 27 patients by inoculation into cultures of monkey kidney cells, haemadsorption becoming evident after 1–2 passages. By means of inhibition of haemadsorption 9 strains were identified as type A 2 and 1 as type B. *D. J. Bauer*

MASON, E. J. & KAUFMAN, N. **The Relationship between Viral Reproduction and Cytotoxicity of Newcastle Disease Virus and Influenza Virus (PR8) in Three Cell Strains.** *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 245–52, 4 figs. [20 refs.]

The authors showed previously [this *Bulletin*, 1961, v. 36, 91] the toxic effect of large doses of Newcastle disease virus (NDV) and influenza (PR8) virus on L and $LLCM_1$ cells of mouse origin and U_{12} cells of human origin. Data are now presented to show that with "small" virus inocula (10 or less egg infectious doses per cell), although virus disappeared more rapidly from cell-free media than from cultures of the 3 cell types, there was no real evidence of multiplication of infectious virus or increase of virus haemagglutinin.

Massive, "toxic", concentrations of virus, inoculated into cell cultures, were removed after 1–2 hours. This removal did not interfere with subsequent cell destruction and allowed initial haemagglutinin values to be determined. There was no increase of infectious NDV or influenza virus. However, haemagglutinin titres of 1 in 128–1 in 512 were obtained in cultures of all 3 cell types infected with influenza virus, maximal in the cells 24 hours after infection and in the supernatant media after 48 hours. Although there was a similar cytopathic effect in cultures infected with NDV, haemagglutinin was not demonstrated, even after treatment with cholera filtrate and sodium periodate, and incubation at 37°C.

D. Taylor-Robinson

DAVENPORT, F. M., ROTT, R. & SCHÄFER, W. **Physical and Biological Properties of Influenza Virus Components obtained after Ether Treatment.** *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 765–82, 3 text figs. & 4 figs. on pl. [35 refs.]

This was a comparative study of 4 human influenza A strains, PR8, FM1, PR301, and AA/23 (Asian) and two animal strains, swine 1976 and the Rostock strain of fowl plague virus. The viruses were fractionated by ether treatment into internal *s* antigen and haemagglutinin. These fractions were morphologically indistinguishable under the electron microscope and in the ultracentrifuge and on electrophoresis and all the haemagglutinins possessed neuraminidase activity though in varying amounts. The haemagglutinin fractions gave the same titres against specific immune sera as did the complete virus and were equally antigenic. Haemagglutinin and *s* antigens produced no toxic effects when given to mice. Extensive complement-fixation (CF) tests were done. Two points of particular interest were that CF tests showed that the purified HA preparations cross-reacted much more in this test than in haemagglutination-inhibition test, and that there were definite serological differences between the *s* antigens which were not "readily explained by the presence of impurities."

D. A. J. Tyrrell

KLEMPERER, H. G. **An Effect of Phloridzin on Influenza Virus Elution and on Neuraminidase Activity.** *Virology.* New York. 1960, Nov., v. 12, No. 3, 495–8, 1 fig.

TOMMILA, V. **Effect of Influenza Antisera on the Enzymatic Action of Five Influenza A Viruses.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 350–54.

FRIDMAN, E. A. **The Heterogeneity of Type A2 Influenza Virus Population.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 274–82, 1 fig. [13 refs.]

Different cultures of the same influenza virus strain (A2 1957 and 1958) showed 3 different types of reaction with non-specific thermostable inhibitors (normal guinea-pig serum) in the haemagglutination reaction. There was either complete elimination of virus haemagglutination (so-called "avid" strains), no change ("non-avid"), or a partial decrease in virus haemagglutinin titre. The latter was assumed to be due to a mixture of "avid" and "non-avid" virus particles and the author attempted to show such heterogeneity by separation of virus strains into 2 pure lines. This was achieved either by infection of chick embryos with limiting dilutions or by inoculation of virus into chorioallantoic membrane tissue cultures in the presence of normal guineapig serum and passage of the surviving virus in chick embryos. 11 virus strains were investigated and substrains, sensitive or insensitive to thermostable inhibitors, were obtained with Singapore/57 and 495 (Leningrad 1957) strains immediately, but more slowly with 1103 and 1104 (Leningrad 1958) strains. Passage did not change the characteristics of the other strains. All 3 types of virus non-specific inhibitor reaction were restored by infecting embryos with a mixture of the 2 lines in different proportion.

A comparison was made between "non-avid" and "avid" lines. The latter eluted less rapidly from chick erythrocytes, reacted with thermostable inhibitors, had a longer latent period in infected chick embryos and were antigenically different in cross haemagglutination-inhibition and absorption tests. *D. Taylor-Robinson*

HEMMES, J. H., WINKLER, K. C. & KOOL, S. M. **Virus Survival as a Seasonal Factor in Influenza and Poliomyelitis.** [Correspondence.] *Nature.* 1960, Oct. 29, v. 188, 430–31, 2 figs.

The survival of influenza virus (PR8) and poliomyelitis virus (CS1 type 1)) was studied at different relative humidities. It was found that influenza virus was rapidly destroyed at relative humidities above 50% and only very slowly below 40%. Poliomyelitis virus, on the other hand, was found to behave in the opposite way, being rapidly destroyed at relative humidities up to 45% and surviving for long periods at humidities above 50%. The authors note that influenza is a winter disease and that in winter relative humidities indoors are low due to the drying effect of room heating. Poliomyelitis is a summer disease when relative humidities are higher.
A. J. Beale

KÖHLER, H., with the technical assistance of I. BAIL, A. ORTMANN & D. SPRINGER. Die Rolle der Leukozyten als Virusträger. [**The Role of the Leucocytes as Virus Carriers**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 140–44.

Leucocytes isolated from chicken blood by a method described elsewhere (KÖHLER and SPRINGER, *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, 264) were maintained in tubes of Parker medium and infected with PR8, Lee, Sendai or Newcastle disease viruses. After incubation for 24 hours in a roller machine a reduction in the haemagglutinin titre of the culture fluid was noted in comparison with a control tube not containing cells. PR8 virus could be recovered from leucocytes obtained from mice 24 hours after intranasal infection, and Newcastle disease virus could be detected in the leucocytes of cocks infected with less than 1LD50 intramuscularly. The results obtained suggest that leucocytes phagocytose virus particles.
D. J. Bauer

TYRRELL, D. A. J., BUCKLAND, F. E., LANCASTER, M. C. & VALENTINE, R. C. **Some Properties of a Strain of SV17 Virus isolated from an Epidemic of Conjunctivitis and Rhinorrhoea in Monkeys *(Erythrocebus patas).*** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 610–16, 9 figs. (8 on 2 pls.) [17 refs.]

KÖHLER, H., with the technical assistance of D. SPRINGER. Neue Wege bei der Isolierung des Poliomyelitisvirus aus dem Blut an Kinderlähmung erkrankter Menschen. Vorläufige Mitteilung. [**New Methods in the Isolation of Poliomyelitis Virus from the Blood of Patients suffering from Poliomyelitis. Preliminary Communication**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 145–6.

The author has utilized the phagocytosis of virus particles by leucocytes described by him [see above] as a means of virus isolation in clinical practice. 17 cc. of blood were taken 5–20 days after the onset of paralysis from 6 patients suffering from poliomyelitis, mixed with 2–3 cc. of 10% citrate solution and centrifuged. The leucocyte layer was removed and washed and the cells were lysed with distilled water; the suspension thus obtained was inoculated into cultures of monkey kidney cells. In all cases poliomyelitis virus was isolated and identified by neutralization tests. *D. J. Bauer*

MCLAREN, L. C., HOLLAND, J. J. & SYVERTON, J. T. **The Mammalian Cell-Virus Relationship. V. Susceptibility and Resistance of Cells *in vitro* to Infection by Coxsackie A9 Virus.** *J. Exper. Med.* 1960, Oct. 1, v. 112, No. 4, 581–94, 1 fig. [28 refs.]

Coxsackie A9 virus does not infect the continuous cell lines that have been tested which are derived from human tissues, whereas it infects primary cultures of human or monkey cells. The authors [this *Bulletin*, 1959, v. 34, 953] have previously shown that the non-primate cells which are resistant to enteroviruses lack a specific cellular receptor responsible for adsorption. They [*ibid.*, 1959, v. 34, 1193] have also shown that infectious RNA from these enteroviruses induces new virus formation both in susceptible and insusceptible cells.

In this paper they show that, during establishment of continuous cell lines, the specific cell receptor substance for Coxsackie A9 virus is lost. This Coxsackie A9

receptor is different from that for poliomyelitis virus or some other enteroviruses. The attachment of Coxsackie A9 to receptor substances or to susceptible cells was enhanced in the presence of calcium or magnesium ions (10^{-3} M calcium or magnesium chloride). Virus attached to cell debris loses its infectivity as previously reported for poliomyelitis virus by the authors [*ibid.*, 1959, v. 34, 953]. However, they also found that both Coxsackie A9 and poliomyelitis virus type 1 could be released from the cell receptor present in frozen and thawed cell debris. For Coxsackie A9 release was effected at *p*H 4·5 in tris buffered gelatin or by 10^{-2} M versene solution, and for poliomyelitis virus at *p*H 2·5. Poliomyelitis virus was not released from cell debris by the following methods: *p*H 7·5–10, ether extraction (known to destroy poliomyelitis virus receptor) [*ibid.*, 1959, v. 34, 953] or fluorocarbon [*ibid.*, 1959, v. 34, 98]. *A. J. Beale*

Beeuwkes, H. **Cytochemistry and Sensitivity of a Human Amnion Cell-Line to Coxsackie A_{23} ($Echo_8$) Virus.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 3, 231–9, 2 figs. [10 refs.]

During the establishment of a continuous cell line from primary human amnion cell cultures it was found that there were clear cut differences between the 2nd and 4th and later transfers. Thus, the 2nd transfer gave a positive staining with Sudan III and the 4th only weak staining. Janus green staining was less intense at early transfers than at later ones. Similarly, alkaline phosphatase reaction was negative at the 2nd passage but strongly positive by the 7th. The morphological appearance also changed, the cells becoming more irregular in shape and containing more nucleoli. It was also found that ECHO 9 virus (alternatively called Coxsackie A 23) susceptibility present at the 2nd passage was lost by the 4th. [See also Pulvertaft *et al.*, this *Bulletin*, 1959, v. 34, 497, and McLaren *et al.*, see above]. *A. J. Beale*

Kantoch, M. & Szalaty, Helena. **The Inhibition of the Phagocytic Activity of Leucocytes by Coxsackie Viruses. III. Viruses inactivated by Ultraviolet Rays.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 3, 399–405. [15 refs.]

"The experiments were concerned with the action of ultraviolet rays on Coxsackie viruses. Coxsackie viruses type A4 and guinea pigs leucocytes were used. *E. coli* 044 served as test bacteria. Irradiation was carried out with LKS 1, S 300. Original Hanau lamp with the distance of 20 cm. from the virus preparation.

"The phagocytic test was used to determine the effect of active and ultraviolet ray-treated viruses on the phagocytic activity of leucocytes. Parallel experiments were performed on 1½–2 days old mouse newborns to find out changes in the virulence of irradiated viral preparations.

"It has been found that the dose of ultraviolet rays which causes a total inactivation of Coxsackie viruses does not suppress their ability to inhibit the phagocytic activity of leucocytes. The viruses irradiated under the given conditions for 30 minutes became avirulent for mouse newborns, but maintained their ability to reduce the phagocytic activity of leucocytes. Prolonged irradiation did not affect the result of experiment.

"These results and those obtained with heat inactivated viruses suggest that the virus component responsible for antileucocytic action of Coxsackie virus is of thermolabile nature. Moreover, the data confirm the assumption of Nishmi and Bernkopf that the action on leucocytes is not related to the multiplication of viruses but to their toxic action."

Rifkind, R. A., Godman, G. C., Howe, C., Morgan, C. & Rose, H. M. **ECHO 9 Virus in Tissue Culture observed by Light and Electron Microscopy.** *Virology.* New York. 1960, Oct., v. 12, No. 2, 331–4, 2 figs.

Gebhardt, L. P. & Hill, D. W., with the technical assistance of G. Dolana & L. P. Gebhardt. **Overwintering of Western Equine Encephalitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 695–8. [13 refs.]

4 garter snakes (*Thamnophis* spp.) were given about 5 log LD50 of western equine virus intraperitoneally [? strain] and killed after 17 days at 4°C.; virus was isolated from the blood of 2 and from the brain of 1 other. 21 garter snakes were given a large dose intraperitoneally then placed in cages buried 3 feet underground outside, with burrows to the surface, in December. Temperatures in the cages ranged from 15–50°F. during the winter compared with −1 to 47°F. above ground. After 19 days the blood of 4 of 5 snakes had virus titres of 1–5 log LD50 in mice. After 64 days the blood of 6 of 8 snakes had virus titres of 1–3 log. After 92 days only 1 of 14 snakes had viraemia (1 log). After 139 days, when the warmer weather had begun, 9 of 14 snakes had viraemia of 1–3·5 log LD50. *C. E. Gordon Smith*

Thomas, L. A. & Eklund, C. M. **Overwintering of Western Equine Encephalomyelitis Virus in Experimentally Infected Garter Snakes and Transmission to Mosquitoes.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 52–5, 1 fig.

The strain of virus used was isolated from *Culex tarsalis* and had undergone 3 mouse passages. 2 species of garter snake (*Thamnophis sirtalis parietalis, T. ordinoides vagrans*) were inoculated intraperitoneally with 6 log LD50. They were placed in a cage with 3 compartments which was dug into the bank of a stream. Each compartment was filled with decayed logs and debris covered with rocks and soil and a layer of straw to provide insulation. Passageways led from the exposed surface to the decayed logs for mosquitoes and snakes. Temperatures during the experiment (November to May) ranged from −24°F. to 84°F. and the medians from 19 to 51°F. 1 compartment contained infected *C. tarsalis* (fed on viraemic chicks) and uninoculated snakes: no viraemia was detected in 25 of these snakes bled 3 times

in March–May. The second compartment contained uninfected mosquitoes and 50 infected snakes: viraemia was detected in 23 of these 26 snakes and 16 of these 23 virus strains were identified as western equine virus. In many instances virus was not detected at the first bleeding soon after recovery from hibernation but after a few days most circulated virus and a titre as high as 6·3 log LD50 was observed. In the 3rd compartment were only infected *C. tarsalis*. No mosquitoes were recovered from any compartment after the winter. By feeding *Culex tarsalis* on 4 hibernating snakes transmission to chicks was effected after an extrinsic incubation period of about 3 weeks. Virus has not yet been isolated from garter snakes collected in the field.

[For a previous study by the authors, see this *Bulletin*, 1959, v. 34, 588. The reference to this paper in the paper abstracted above is incorrectly cited.]

C. E. Gordon Smith

ISHIGA, A., OHYAMA, A. & HOTTA, S. **Cultivation of Japanese B Encephalitis Virus in Hamster Kidney Cell Cultures.** *Japanese J. Microbiol.* 1960, Jan., v. 4, No. 1, 53–9, 3 figs. [18 refs.]

The Nakayama and GI strains of Japanese encephalitis virus were used at high mouse-passage levels. Trypsinized hamster kidney cells grew first an epithelium-like sheet after 5–7 days: this degenerated and left a fibroblastic sheet which could be maintained for 3 weeks or more: in this work cultures of the latter type were used. Incubation after inoculation was at 37°C. After infection with about 50 LD50 of GI strain a maximum virus titre in the cultures was present 3–5 days after inoculation, this period coincided with the development of cytopathic changes. 25 serial passages in culture were successfully achieved with a final titre of 4·5 log mouse intracerebral LD50/0·02 ml. Neutralization tests were successful with the tissue culture system and the virus after passage was thus identified.

Titrations [? material] carried out in parallel in culture and by intracerebral inoculation of mice showed that titres in hamster kidney cultures were 1·5–2·0 log higher.

C. E. Gordon Smith

VERMEIL, C., LAVILLAURBIX, J. & REEB, E. Sur la conservation et la transmission du virus West Nile par quelques arthropodes. **[Survival and Transmission of West Nile Virus by Various Arthropods]** *Bull. Soc. Path. Exot.* 1960, Mar.–Apr., v. 53, No. 2, 273–9. [11 refs.]

Arthropods were infected by feeding on viraemic mice or chicks infected with the 28B strain of West Nile virus. Culicines were kept at 25°C. and 90–100% humidity after infection. Transmission was by feeding on mice or chicks: brains from animals which did not develop symptoms were passaged to mice and KB cell-cultures. Animals [? the latter] which did not develop symptoms were challenged intraperitoneally with West Nile virus. With *Aedes aegypti* infection was established and transmission achieved after 10–15 days' extrinsic incubation. With *Aedes geniculatus* transmission was effected after 6 days' extrinsic incubation. With *Anopheles punctor*, *Anoph. plumbeus* and *Culex fatigans* similar results were obtained. With nymphs of *Triatoma infestans* virus was demonstrated in an emulsion after 2 days' incubation but transmission failed after 35 days' extrinsic incubation. Virus was not recovered from *Leptopsylla segnis* or from 10 larvae and 2 nymphs of *Tenebrio molitor* inoculated with virus. Nymphs of *Ornithodorus coniceps* infected on a variety of animals transmitted 35 days—10 months after infection but the majority of infections were inapparent in mice. *O. erraticus* infected as nymphs transmitted (inapparent infection) after 45 days but *O. moubata* did not and virus could not be demonstrated by inoculation of a suspension into mice.

C. E. Gordon Smith

SALMINEN, A. **Adsorption onto and Elution from Erythrocytes of the Tick-Borne Encephalitis Virus.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki, 1960, v. 38, No. 3, 267–80. [10 refs.]

The Belyanchikov strain of biphasic tick-borne encephalitis virus was used and propagated in suckling mice. A 10% extract of suckling mouse brain in *p*H 9·3 buffer had a haemagglutinin titre of 1:25,600 at *p*H 6.5, +4°C with 0·2% rooster erythrocytes. The adsorption experiments were assayed by intracerebral mouse titration. Under conditions where the fluid contained 10^8 mouse LD50 of virus and 10^8 erythrocytes per ml. maximum adsorption of virus to cell occurred at *p*H 6·5: after adsorption at ice temperature the cells were washed 3 times with 40 volumes then suspended in borate buffered albumin (*p*H 9)—7·5 log LD50 per 0·03 ml. were eluted at *p*H 6·5. Adsorption was 25 times greater at 0°C. than at 37°C. With only 1 erythrocyte per 5 LD50 of virus adsorption was less than with equal numbers. Elution occurred equally well at *p*H 7·4 or 9·0 and at 0°C. or 37°C. Adsorption appeared to be complete in 15 minutes and elution in 5 minutes. Adsorption with cells reduced the virus content of fluids by about 60% even when 25,000 erythrocytes per LD50 were used. Only insignificant amounts of virus were removed from cells by repeated washing at the adsorption *p*H. 10 successive adsorptions with erythrocytes only reduced the infectivity of the original by 1·0 log (*i.e.*, by 90%). This is believed to be due to the presence of haemagglutinin inhibitors as 98% of virus could be adsorbed from a brain suspension of virus extracted with acetone [this *Bulletin*, 1959, v. 34, 400]. The same erythrocytes could adsorb virus at least twice and goose erythrocytes appeared to be as effective as rooster cells.

C. E. Gordon Smith

SALMINEN, A. **Removal of Tick-Borne Encephalitis Virus Receptors from Erythrocytes by Extraction with Lipid Solvents.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 281–7. [10 refs.]

Extracts of rooster cells by various solvents were tested for haemagglutinin-inhibiting activity against a sucrose-acetone antigen of the Belyanchikov strain of tick-borne

encephalitis virus: methanol, ethanol, chloroform-methanol (3:1), ethanol-ether (3:1), and acetone gave inhibitory extracts titring 1:1280–1:640, while chloroform, light petroleum and ether gave titres of 1:80–1:40. Most of these extracts caused agglutination of cells in higher concentrations. The extracted cells were spontaneously agglutinable. Acetone extracted cells adsorbed 1·2 log LD50 less and those extracted with ethanol and ether 1·7 log less virus than untreated [see above]. Acetone extracted cells adsorbed only one-eighth–one-sixteenth of the haemagglutinin adsorbed by unextracted cells.

[The claim that the inhibitor extracted by solvents is the cell-receptor material because the damaged (extracted) cells are less able to adsorb virus, does not seem to be proved by the evidence presented.]

C. E. Gordon Smith

Ovchinnikova, L. D., Ponomarenko, N. I. & Sonchik, N. A. **The Production of Brain Vaccine against Tick-Borne Encephalitis.** *Problems of Virology.* London. 1959, v. 4, No. 5, 56–9. [Translated from Russian.]

Mouse-brain vaccines were prepared with the Sof'in and L-z strains of tick-borne encephalitis and the Absettarov strain of biphasic meningo-encephalitis viruses. 160 mice on average yielded 1 litre of vaccine. Most (89%) inoculated mice sickened 4 days after inoculation but where virus titres were compared on the 4th day between mice with and without symptoms no significant difference could be demonstrated. Similarly no difference in potency could be demonstrated between vaccines prepared from brains of mice killed on the 4th day with symptoms, and similar mice whether or not they had symptoms. All mouse brains for vaccine production may therefore be safely harvested on the 4th day.

C. E. Gordon Smith

Levkovich, Y. N., Zasukhina, G. D., Chumakov, M. P., Lashkevich, V. A. & Gagarina, A. V. **Tissue Culture Vaccine against Tick-Borne Encephalitis.** *Problems of Virology.* London. 1960, v. 5, No. 2, 253–7. [Translated from Russian.]

The Pan strain of tick-borne encephalitis virus isolated from a patient with mild disease was used [? passage level]. It was grown in chick-embryo monolayer cultures. The fluid was harvested after 96–100 hours, centrifuged at 11,000 r.p.m. [? in a Sharples-type centrifuge] then filtered. Formaldehyde to a concentration of 1:2000 was then added and the vaccine held at 37°C. for 72 hours with tests at intervals for live virus after neutralization of the formalin with sodium bisulphite. After 72 hours a safety test was made on 550 ml. and during this the vaccine was held at 2–4°C. The *p*H was then adjusted to 8·0 and aluminium hydroxide added. After 24 hours at 4°C. half the supernatant was decanted, the sediment shaken up and the vaccine tested for potency.

Titrations in cynomologus heart (CMH) cell-cultures and by intracerebral inoculation of mice gave similar infectivity titres (about 7 log LD50 or TCD50 per ml.) before and after centrifugation and filtration. Formalin inactivation was shown to be complete after 6 hours. The safety test involved inoculation of 100 mice with 0·5 ml. deformalinized vaccine intraperitoneally and 0·03 ml. intracerebrally. Blind passages on groups of mice were made at intervals. In the potency test mice were given 3 subcutaneous doses of 0·5 ml. at 2-week intervals then challenged 14 days later with the Absettarov strain. The vaccine before addition of aluminium hydroxide had a protective index of 2,400, after aluminium hydroxide adsorption it was 15,000. After 5 months' storage it was 160,000. The sera of immunized mice were tested in CMH cells against the Sof'in strain: 15 days after vaccination, mice given unadsorbed vaccine had no antibody while those given aluminium hydroxide adsorbed vaccine had a titre of 32: both groups had high titres 30 days after vaccination. 20 persons who had been previously vaccinated with mouse-brain vaccine were revaccinated with the tissue-culture vaccine. No reactions occurred and 3 weeks after vaccination their sera were tested in an intracerebral mouse neutralization test against the Khabarovsk-17 strain from the Far East. The majority (6 of 9 in which paired sera were tested) had a good antibody response.

C. E. Gordon Smith

Sergiyenko, A. D. **Technique of Performing the Haemolysis Reaction in Haemorrhagic Nephroso-Nephritis. (Synonym: Haemorrhagic Fever with Renal Syndrome.)** *Problems of Virology.* London. 1960, v. 5, No. 1, 121–3. [Translated from Russian.]

Hitchcock, Griselda & Isaacs, A. **Protection of Mice against the Lethal Action of an Encephalitis Virus.** *Brit. Med. J.* 1960, Oct. 29, 1268–70. [10 refs.]

The authors have previously shown that interferon is produced in the lungs of mice during the course of infections with influenza virus [this *Bulletin*, 1960, v. 35, 1056]. It is also known that interferon prepared in tissue culture will protect rabbits against a cutaneous infection with vaccinia virus [*ibid.*, 1960, v. 35, 200]. In this paper experiments are described in which mice were partly protected from the lethal effect of a generalized infection induced by a small dose of Bunyamwera virus given intraperitoneally. Interferon was prepared in tissue cultures or extracted from the lungs of mice infected with influenza and given intraperitoneally before and with the Bunyamwera virus. Finally it was found that if mice were inoculated intranasally with a relating avirulent strain of influenza A (Kunz) then they were partly protected from the effect of Bunyamwera virus given the next day. It is argued that this was the result of "endogenous" interferon produced in response to the influenza virus infections, and that interferon might be used to prevent infections in man without impairing natural defence mechanisms, such as antibody production.

D. A. J. Tyrrell

De Maeyer, E. **Plaque Formation by Measles Virus.** *Virology.* New York. 1960, July, v. 11, No. 3, 634–8, 1 fig.

The author has developed a method for obtaining plaques with measles virus in continuous cell lines. Monolayers established in bottles in Eagle's medium with 10% calf serum were seeded with virus and subjected to mechanical shaking at 60 cycles per minute for 2 hours at 37°C. The fluid was then removed and replaced with an overlay of 3% agar in Hanks solution with an equal part of nutrient fluid consisting of 90% amniotic fluid and 10% horse serum. The agar suspension at 42°C. was mixed with the nutrient fluid at 37°C. and poured immediately. After incubation for 5 days a second overlay was added; on the 6th day 0.5 cc. of 1:2000 neutral red in isotonic phosphate buffer solution was added and further incubation was carried out in the dark. With the Edmonston strain of measles virus adapted to human amnion cells the plaques were large enough to be counted on the 7th day and increased in number until the 10th day. By this method plaques could be obtained in HeLa cells and the WS continuous line of human amnion cells as well as in primary explants of human amnion. Plaques were produced in chick embryo monolayers by the egg-adapted strain of virus.

D. J. Bauer

Musser, S. J. & Underwood, G. E., with the technical assistance of S. D. Weed & J. L. Ossewaarde. **Studies on Measles Virus. II. Physical Properties and Inactivation Studies of Measles Virus.** *J. Immunology.* 1960, Sept., v. 85, No. 3, 292–7, 2 figs. [18 refs.]

Measles virus in the form of infected tissue culture fluid declined in titre from 4·9 log units to zero during storage for 54 weeks at 6°C.; in the presence of 5% calf serum the titre after the same period was 2·8 log units. There was little advantage in storage at −30°C., but at −72°C. the fall in titre was much reduced. The virus withstood freeze-drying and subsequent storage at 6°C. for 18 months with little fall in titre provided that 5% calf serum was present in the medium before drying. The rate of thermal inactivation at 25°, 37°, 45° and 56°C. was studied. In an investigation of the effect of *p*H at 25°C. it was found that infectivity was retained for 3 hours at *p*H 7 and *p*H 8, fell slightly at *p*H 5, *p*H 6, or *p*H 9, and fell to zero after 3 hours at *p*H 10. The virus could be filtered through sintered glass, sintered stainless steel or millipore filters, and could be deposited by centrifugation for 2 hours at 40,000 r.p.m. It was rapidly inactivated by exposure to beta or gamma radiation.

[For Part I, see this *Bulletin*, 1960, v. 35, 719.]

D. J. Bauer

IMMUNITY

Raffel, S. **Aspects of Contemporary Research in Immunology.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 461–8, 3 figs. [29 refs.]

In this, the fifth J. Burns Amberson Lecture [delivered to the National Tuberculosis Association and its medical section, the American Thoracic (formerly Trudeau) Society], the author establishes the existence of a special kind of rapport between concepts and information gleaned from investigations of interactions between mycobacteria and their hosts, and developing knowledge in other areas of immunology. On the origin and nature of antibodies he points out 3 methods of approach: (a) the study of disease states in which hyperglobulinaemia occurs, (b) the reverse situation, where in hypogammaglobulinaemia there is also a failure of synthesis of antibodies, and (c) the study of antibody molecules tagged with a fluorescent substance. This leads to a mention of the Ehrlich "side-chain" theory and the alternative view of a process for cellular instruction. After dealing with immunological activity at various stages throughout the life-span, referring to immunological tolerance and immunological paralysis, the author reviews some of the conditions in which an individual may respond immunologically against his own constituents to produce destructive disease, in violation of the "law" of self-preservation and of the immunological axiom of self-recognition.

D. A. Cannon

Gourwitch, G., with the collaboration of G. Chouma-kowa. L'activité immunologique des organes lymphoïdes et les principes généraux de l'immunogenèse. [**Immunological Activity of Lymphoid Tissue and the General Principles of Immunogenesis**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 530–49, 5 figs. [24 refs.]

After a brief historical survey of work done on lymphoid tissue in relation to the formation of antibodies and the establishment of immunity, the author describes her work on the immunization of guineapigs and rabbits with soluble and insoluble antigens. The cellular changes (in the plasmocyte line) following the introduction of a soluble antigen occurred only in the regional lymph node; those following the injection of an insoluble antigen had a much wider distribution, involving remote lymph glands. Antibody titrations in the lymph node and serum were similar. Some adjuvant emulsions give to soluble antigens some of the characteristic properties of insoluble antigens. Functional exhaustion of the lymphoid tissue can occur; no response results from an antigenic stimulus and there is immunological inhibition.

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has varied, depending upon many factors, the response being better in the young, those without antibody, when other enterovirus excretion is rare, when the viruses are given singly and in large doses up to 10^7 TCD50 per ml. Many trials have been initiated throughout the world, although rather few up to the present have been organized by scientists independent of the three originators of attenuated virus strains. These trials have varied in thoroughness of follow-up but none have shown any untoward effects. At present none have shown that the vaccine is effective in preventing poliomyelitis. There can, however, be little doubt that the vaccine will prove effective in those in whom virus multiplies and produces an antibody response.

[This is much too long and detailed a report to abstract fully. It is a mine of information about living polio-vaccine both factual and theoretical.] *A. J. Beale*

TURNER, R. **Live Attenuated Poliovaccine. A Review.** *South African Med. J.* 1960, Nov. 12, v. 34, No. 46, 961–6. [20 refs.]

KOPROWSKI, H. **Tin Anniversary of the Development of Live Virus Vaccine.** *J. Amer. Med. Ass.* 1960, Oct. 22, v. 174, No. 8, 972–6. [13 refs.]

Dr. Koprowski has again presented an amusing and instructive account of the development of attenuated poliomyelitis vaccine from the beginnings in 1950 when he infected a few susceptible subjects with the TN type 2 strain till 1960 when, at the meetings in Washington, over 60 million people were reported to have had attenuated poliomyelitis vaccine. Originally chance mutations had to be selected whereas now the possibility of increasing mutation rates by changing the composition of the nucleic acid with nitrous acid has been demonstrated. The author is convinced of the safety and efficacy of attenuated poliomyelitis vaccine and looks forward to many more anniversary celebrations.

There are some problems still outstanding. Newborn infants respond poorly [PAGANO *et al.* this *Bulletin*, 1961, v. 36, 61]. Interference occurs if all 3 strains are given together or if other enteroviruses are prevalent. Stability of strains in any absolute sense is plainly an impossibility with a replicating agent susceptible to mutation. This admitted, Koprowski denies the importance of such changes for the properties of greatest interest—safety and efficacy.

The presence of extraneous viruses in the attenuated poliomyelitis vaccine is a serious problem although Koprowski believes it has been overemphasized. It is thought that the problem might be overcome by (a) removal of simian viruses by differential adsorption onto ion exchange columns, (b) use of stable early passage human cell lines or (c) the use of infectious RNA in non-primate cells which are not susceptible to the intact poliomyelitis virus. *A. J. Beale*

GEFFEN, T. J. **Poliomyelitis in Vaccinated Subjects, England and Wales, 1959.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Nov., v. 19, 196–8.

(L/191)

GEFFEN and SPICER [this *Bulletin*, 1960, v. 35, 1126] have previously reported the cases of poliomyelitis occurring in persons vaccinated against poliomyelitis in 1958 with an assessment of the efficacy of the vaccine. Now, provisionally, figures for 1959 are presented. There were 1028 notified cases of poliomyelitis of which 739 were paralytic. 33 paralysed patients had had 1 dose of vaccine, 75 2 doses and 40 3 doses. 12 paralysed patients had disease involving the inoculated limb within 27 days of vaccination and another 22 patients were also paralysed within 27 days of vaccination but without involvement of the inoculated limb. The effectiveness of poliomyelitis vaccine was estimated for children under 15 years by calculating attack rates assuming the vaccination status to be that of the population when 50% of the notifications had been made. On this basis the rates per 100,000 for vaccinated and non-vaccinated individuals respectively were as follows: all cases (paralytic and non-paralytic), 2·7 and 16·9; paralytic only, 1·8 and 12·2; and, excluding those with 1 dose from the vaccinated group, 1·4 and 12·4 for paralysed patients. The ratio of paralytic to non-paralytic patients was reduced with increasing numbers of doses being: no vaccine, 2·9; 1 dose, 3·0; 2 doses, 1·9; 3 doses, 1·25. *A. J. Beale*

SPEERS, J. F., CHIN, T. D. Y., MARINE, W. M., HALL, E. C. & GRAVELLE, C. R. **Epidemic Poliomyelitis, Des Moines, Iowa. 1959. Preliminary Report.** *J. Amer. Med. Ass.* 1960, Oct. 15, v. 174, No. 7, 864–8, 3 figs.

There was a severe epidemic of poliomyelitis in Des Moines, Iowa, in 1959 which followed a similar pattern to the epidemics in Chicago in 1956 [NATHANSON *et al.*, this *Bulletin*, 1960, v. 35, 1016] and Detroit in 1958 [BROWN *et al.*, *ibid.*, 1960, v. 35, 677]. These major epidemics have all occurred since the widespread use of Salk poliomyelitis vaccine, although it is as yet uncertain that this is the only factor concerned in the differences between these epidemics and earlier ones. There were 134 cases within the city limits, 53 of which were paralytic. Type 1 poliomyelitis was mainly responsible for the paralytic cases. Evidence for ECHO, Coxsackie and type 3 poliomyelitis virus infection, as well as for poliomyelitis virus type 1 infection, was found among non-paralytic cases. The rates for paralytic poliomyelitis were 3·1 per 100,000 for upper, 29·2 for middle and 58·0 for lower socio-economic groups. The highest incidence was at age 0–4 years but in the 1952 and 1954 epidemics it had been at 5–9 years. The rate for paralytic cases was 20·2 for whites and 136 for Negroes. These epidemiological features were not seen prior to 1956.

In the age-group 0–14 the incidence of paralytic poliomyelitis was 216 per 100,000 for unvaccinated individuals and 20·0 for those who had had 3 doses giving an effectiveness of 90%. Also, the severity of the residual paralysis was less in vaccinated subjects. Thus, 7 out of 17 who had had 3 or more doses made a complete functional recovery whereas only 11 out of 70 patients who had had less than 3 doses did so.

[A more detailed study of the epidemic is promised soon.] *A. J. Beale*

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Cook, G. T. & Smith, A. J. **Serum Neutralizing Antibodies to Coxsackie B Viruses.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Sept., v. 19, 165–9.

4 groups of sera were examined for the presence of antibodies to the first 5 members of the Coxsackie B virus group. Series A sera comprised 100 samples from children sent to the Streptococcal Reference Laboratory of the Public Health Laboratory Service for streptolysin titre. Series B were 100 antenatal sera from Surrey. Series C were 50 sera from venereal disease and maternity clinics in Newport, Monmouthshire and Series D were from 50 blood donors in Leeds. The differences between groups B, C and D were slight. The incidence of antibodies at a dilution of 1/20 for Series A and Series B, C and D, respectively, were as follows: type 1, 11% and 18·5%; type 2, 27% and 59%; type 3, 42% and 28%, type 4, 50% and 62%; type 5, 6% and 14·5%. In general, children had higher titres than adults. This was most noticeable for type 3 and there had been an increased type 3 prevalence just prior to the collection of the sera. The authors conclude that antibodies to the Coxsackie B viruses are probably not uncommon in the general population. [The sera were admittedly not collected in a satisfactory way to give a representative sample of the population.] *A. J. Beale*

De Góes, P., De Paola, D., Bruno-Lobo, M. & Dias, L. D. Miocardite por vírus Coxsackie do grupo A. **[Myocarditis produced by Coxsackie Virus Group A]** *Anais Microbiol.* Rio de Janeiro. 1959, v. 7, 13–34, 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"Two cases of acute myocarditis in sibling children occurring at the same time are described. One of them died after a short period of illness and at autopsy, lesions suggesting viral myocarditis were observed. In the other case the same diagnosis was established according to the clinical, radiographic and eletrocardiographic data, but the child recovered after four months of illness. In this case a Coxsackie group A type 4 virus was isolated from the stools. This strain when inoculated in baby and adult mice revealed cardiotropism producing focal myocarditis."

Tilley, J. H. MacD. **Infective Hepatitis in a Mixed School, with High Attack Rate in Females.** *Brit. Med. J.* 1960, Nov. 5, 1354–6, 1 graph.

A small epidemic of infective hepatitis from January to June 1959 was centred on a mixed non-residential school in an urban district, where 27 of the cases occurred. There was no excess of girls over boys in the school; yet 23 of the 27 school cases were in girls and only 4 in boys.

There is no evidence that females usually preponderate in the sex incidences of this disease. The apparent explanation for the anomaly in this instance was temporary inadequate toilet accommodation in the school, especially affecting girls. The epidemiological evidence favoured bowel-to-mouth transmission of the infection; although poliomyelitis vaccination was in progress during the period there was no evidence of syringe-transmitted infection.

H. Stanley Banks

Singh, H. N. **Neomycin in Infective Hepatitis.** *Indian Practitioner.* 1959, Dec., v. 12, No. 12, 1035–44, 4 figs.

This is a description of 30 cases of infectious hepatitis treated with neomycin, glucose, and vitamins. Neomycin acts on the bacterial flora of the intestine and prevents or reduces ammonia formation. On certain experimental evidence this is supposed to protect the liver cells from the destructive action of organisms.

The author considers that improvement in the symptoms and signs was remarkable. [This is, however, a subjective judgment, justification for which is not very obvious from the data. It is possible that a controlled trial might demonstrate no beneficial effect from this treatment.]

H. Stanley Banks

Tiszai, A., Faredin, I. & Acsai, P. Über die Wirkung des Ephedrins auf die 17-Ketosteroid-Ausscheidung bei der Hepatitis epidemica **[The Influence of Ephedrine on 17-Ketosteroid Excretion in Epidemic Hepatitis]** *Wien. med. Woch.* 1960, Nov. 12, v. 110, No. 45, 924–6, 3 figs. [31 refs.]

In this paper the authors refer to some of the observations on the effects of cortisone and ACTH [corticotrophin] and of ephedrine in epidemic hepatitis, which have led to the assumption that ephedrine has the property of mobilizing ACTH and influences the pituitary-adrenal system.

Studies were made on 16 patients suffering from epidemic hepatitis and 8 healthy controls to determine the effect of ephedrine on the urinary excretion of 17-ketosteroids and the eosinophil blood count. The results are described with diagrams.

Ephedrine by mouth (0·10 gm. and succeeding doses of 0·05 gm. every 2 hours) brought about a 50% reduction in the eosinophil count in 4 hours in both patients and controls. The low urinary excretion of 17-ketosteroids of the patients was increased by ephedrine and gradually reached normal values whereas such increase did not appear in the controls. The authors assume that this increase of 17-ketosteroids excretion in hepatitis is not associated with the adrenal effect of ephedrine but may be attributed to an eventual beneficial influence of the drug on the liver function. *M. E. Delafield*

Blanc, G., Ascione, L. & Mailloux, M. Les petits mammifères sauvages peuvent-ils être porteurs du virus de la chorioméningite lymphocytaire? Enquête faite au Maroc. **[Can Small Wild Mammals Harbour Lymphocytic Choriomeningitis Virus? Investigations in Morocco]** *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 27/28, 645–9, 5 figs.

During the examination of several species of small mammals wild-caught in Morocco for leptospiral and

ROSS, Ann; LEPOW, I. H. **Studies on Immune Cellular Injury. I. Cytotoxic Effects of Antibody and Complement** [ROSS & LEPOW]. *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1085–106, 1 fig. [46 refs.]. **II. Functional Role of C'1 Esterase in Immune Cytotoxicity** [LEPOW & ROSS]. *Ibid.*, 1107–20. [14 refs.]

ROANTREE, R. J. & COLLIS, L. R. **Effect of the Peritoneal Fluid of the Guinea Pig on Strains of Enteric Bacilli.** [Correspondence.] *Nature.* 1960, Sept. 17, v. 187, 1045–6.

[During the Great War WRIGHT and his colleagues (*Lancet*, 1918, v. i, 831) reported experiments which suggested that bacteria from war wounds could be grouped according to their ability to grow freely from small inocula in fresh human serum. Those which grew freely included strains of streptococci and *Staphylococcus aureus* and were called "serophytes" and those which failed to grow, strains of coliform bacilli, were called "sero-saprophytes". It seemed likely that the difference between the two groups was related to the sensitivity of the organisms concerned to the bactericidal effect of normal serum which depended on complement.]

More recent observations on the Gram-negative intestinal bacilli are somewhat conflicting but it appears that there is considerable variation in the sensitivity of different strains of this group of organisms to the bactericidal effect of normal sera. In the present paper the authors show that with 11 strains of *Escherichia coli* there were 5 sensitive to the bactericidal action of fresh normal sera, both from human sources and the guineapig and 6 were resistant. In addition they found that when such strains were implanted in permeable containers in the peritoneal cavity of the guineapig the most sensitive strains were killed by the bactericidal action of the peritoneal fluid whereas the most resistant strains not only survived but multiplied. The results with intermediate strains were variable. The authors' findings support the thesis that the complement-dependent bactericidal system is of importance in limiting the number of strains capable of surviving *in vivo* in tissue fluids.

[In principle these results are in agreement with the results of LOWBURY and RICKETTS [this *Bulletin*, 1957, v. 32, 1010] with regard to the part played by the properdin system in burns infections. They found that the sera of burned patients contained a reduced level of properdin as compared with normal sera. *Pseudomonas pyocyanea*, *Proteus* and *Klebsiella* are commonly found in burns whereas *E. coli* is uncommon. In their experience *E. coli* was usually highly sensitive to the bactericidal of normal serum but *Ps. pyocyanea*, *Proteus* and *Klebsiella* are generally resistant or only slightly sensitive. The origin of the strains examined by the authors of the paper under review is not stated but it is presumed that they were not isolated from burns; it is probable that strain-variation is important.] The paper contains an interesting description of the small permeable chambers used for testing the effect *in vivo* of the bactericidal activity of the peritoneal exudate of the guineapig on the various strains of gram-negative bacilli.

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"Interferon and rabbit antibody placed in beads on an agar overlay of infected cells give zones of protection against plaque-forming viruses. From the size of the protection zones obtained with different times of application, the diffusion coefficient of antibody and interferon can be calculated. The figures obtained for antibody are lower than accepted values; possible reasons for this are given. The diffusion coefficient of interferon appears to be much higher than that of rabbit antibody, and it is concluded that the molecular weight of interferon is less than 80,000."

COLOBERT, L. & KIRN, A. Un nouveau facteur lytique du sérum sanguin humain normal: l'obsistine. **[Obsistin, a New Lytic Factor in Norman Human Serum]** *C.R. Soc. Biol.* 1960, v. 154, No. 3, 600–602. [10 refs.]

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SHEPARD, C. C. **Phagocytosis of Micro-organisms by HeLa Cells. I. The Use of Bovine Fetal Serum for the Study of Mycobacteria and Certain Other Gram-Positive Bacteria.** *J. Immunology.* 1960, Oct., v. 85, No. 4, 356–60. [12 refs.] **II. Serum Activities Resembling Properdin.** *Ibid.*, 361–7. [18 refs.]

I. "1. Bovine fetal serum promotes the uptake of mycobacteria by HeLa cells and has been found superior to horse serum and chicken serum in infection medium. There has been little variation between lots.

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horse serum. Absorption with Zymosan of the bovine fetal serum before its inclusion in infection medium leads to more rapid intracellular growth of these organisms. Dilution of these organisms in broth, rather than salt solution, also increases the rate of their subsequent intracellular growth.

"4. A combination of two purified proteins, bovine fetuin and human albumin, also promotes the uptake of mycobacteria, staphylococci, and group A streptococci. A medium containing these two proteins appears to be the preferable infection medium for the growth of these organisms in HeLa cells."

II. "1. The activity of different species of animal sera in controlling the species of microorganism taken up by HeLa cells may be divided into two types on the basis of stability to heat, absorbability by Zymosan at 17°C., comparative activity of bovine fetal serum, and the species of microorganism acted upon.

"2. Activity that is promoted by bovine fetal serum is also promoted by some lots of horse serum and concerns mycobacteria, staphylococci and group A streptococci. The activity is duplicated by a combination of purified preparations of bovine fetuin and human albumin.

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"4. A mixture of fresh and inactivated chicken serum promoted uptake of all the microorganisms. Following absorption with Zymosan, the activity was limited to the species in the first group, namely, mycobacteria, staphylococci, and group A streptococci.

"5. The absorption to Zymosan of the activity of dog serum for *P. tularensis* had requirements for temperature, ionic strength and Mg^{++} that resemble closely those described for the reaction between properdin and Zymosan. Treatment of dog serum by methods designed to destroy C′1, C′2, and C′4 caused loss of its phagocytosis-promoting activity. The chicken serum activity for *P. tularensis* and the guinea pig serum activity for *Br. suis* had similar but somewhat different properties. Absorption of the guinea pig serum with Zymosan did not remove its activity for *H. capsulatum*, although it did remove that for *Br. suis*.

"6. Rendering the HeLa cell line free of PPLO did not change its behavior in phagocytosing bacteria."

ASKONAS, B. A., FARTHING, C. P. & HUMPHREY, J. H. **The Significance of Multiple Antibody Components in Serum of Immunized Rabbits.** *Immunology*. Oxford. 1960, Oct., v. 3, No. 4, 336–51, 6 figs. [34 refs.]

See also p. 271, GODFREY, PARSONS & RAWSTRON. **Rapid Destruction of Antitetanus Serum in a Patient Previously Sensitised to Horse Serum.**

Book Review

HERRLICH, A., with the collaboration of A. MAYR. **Die Pocken: Erreger, Epidemiologie und klinisches Bild.** [The Pox Diseases: Viruses, Epidemiology and Clinical Aspects] With an introduction by E. RODENWALD. pp. xii + 295, 52 text figs. & 34 pls. (19 coloured). 1960. Suttgart (14a): Georg Thieme Verlag, Herdweg 63, Germany. [DM 64.-.]

Smallpox is virtually unknown to the present generation of medical practitioners in Western countries, and a disease which was once a ubiquitous infection has long since been confined to the tropics. However, with the development of air travel, communication with the endemic areas has been greatly intensified, and with it the risk of introducing smallpox into countries which are virtually unprotected has been greatly increased. At any time, therefore, the medical profession in these countries is liable to be confronted with an epidemic of a disease with which it is largely unfamiliar. It is with this in mind that Professor Herrlich has written his monograph on the pox diseases, and he has produced a work which should be readily available to any member of the profession who feels that his knowledge of the subject is in need of enlargement.

The book is in 3 parts. The first deals with the laboratory aspects of the pox viruses which infect man, including vaccinia, alastrim, variola major, cowpox and paravaccinia. The second, which is the major part of the book, deals with smallpox in all aspects, including accounts of the epidemics in Glasgow, Vannes and Heidelberg in recent years. In the final part the pox diseases of animals and birds are described, and the book is concluded with a magnificent atlas of smallpox in all its manifestations in 34 plates, many of which are coloured. The main criticism which can be levelled against this otherwise uniformly excellent work is that the complications of vaccination such as generalized vaccinia, eczema vaccinatum, vaccinia necrosum, etc., are described only briefly. Although they are rare conditions, they are of great importance as iatrogenic diseases with a high mortality, and anyone who turns to Prof. Herrlich's monograph to find information on them will be disappointed not to find them discussed in greater detail. The section on animal pox diseases would also benefit from the inclusion of contagious dermatitis and lumpy skin disease. These are minor criticisms, however, and are only prompted by the high standard which the author has set himself. The book is beautifully produced and in appearance and scientific content is well worth its high price.

D. J. Bauer

Printed in Great Britain by The Eastern Press, Ltd., London and Reading

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D. A. Cannon

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"3. Activities that are not promoted by bovine fetal serum are in most cases absorbable by Zymosan or heat labile. Included in this type is the action of dog serum toward *Pasteurella tularensis*, and guinea pig serum toward *Brucella* and *Histoplasma capsulatum*.

"4. A mixture of fresh and inactivated chicken serum promoted uptake of all the microorganisms. Following absorption with Zymosan, the activity was limited to the species in the first group, namely, mycobacteria, staphylococci, and group A streptococci.

"5. The absorption to Zymosan of the activity of dog serum for *P. tularensis* had requirements for temperature, ionic strength and Mg^{++} that resemble closely those described for the reaction between properdin and Zymosan. Treatment of dog serum by methods designed to destroy C'1, C'2, and C'4 caused loss of its phagocytosis-promoting activity. The chicken serum activity for *P. tularensis* and the guinea pig serum activity for *Br. suis* had similar but somewhat different properties. Absorption of the guinea pig serum with Zymosan did not remove its activity for *H. capsulatum*, although it did remove that for *Br. suis*.

"6. Rendering the HeLa cell line free of PPLO did not change its behavior in phagocytosing bacteria."

ASKONAS, B. A., FARTHING, C. P. & HUMPHREY, J. H. **The Significance of Multiple Antibody Components in Serum of Immunized Rabbits.** *Immunology*. Oxford. 1960, Oct., v. 3, No. 4, 336–51, 6 figs. [34 refs.]

See also p. 271, GODFREY, PARSONS & RAWSTRON. **Rapid Destruction of Antitetanus Serum in a Patient Previously Sensitised to Horse Serum.**

Book Review

HERRLICH, A., with the collaboration of A. MAYR. **Die Pocken: Erreger, Epidemiologie und klinisches Bild.** [The Pox Diseases: Viruses, Epidemiology and Clinical Aspects] With an introduction by E. RODENWALD. pp. xii + 295, 52 text figs. & 34 pls. (19 coloured). 1960. Suttgart (14a): Georg Thieme Verlag, Herdweg 63, Germany. [DM 64.-.]

Smallpox is virtually unknown to the present generation of medical practitioners in Western countries, and a disease which was once a ubiquitous infection has long since been confined to the tropics. However, with the development of air travel, communication with the endemic areas has been greatly intensified, and with it the risk of introducing smallpox into countries which are virtually unprotected has been greatly increased. At any time, therefore, the medical profession in these countries is liable to be confronted with an epidemic of a disease with which it is largely unfamiliar. It is with this in mind that Professor Herrlich has written his monograph on the pox diseases, and he has produced a work which should be readily available to any member of the profession who feels that his knowledge of the subject is in need of enlargement.

The book is in 3 parts. The first deals with the laboratory aspects of the pox viruses which infect man, including vaccinia, alastrim, variola major, cowpox and paravaccinia. The second, which is the major part of the book, deals with smallpox in all aspects, including accounts of the epidemics in Glasgow, Vannes and Heidelberg in recent years. In the final part the pox diseases of animals and birds are described, and the book is concluded with a magnificent atlas of smallpox in all its manifestations in 34 plates, many of which are coloured. The main criticism which can be levelled against this otherwise uniformly excellent work is that the complications of vaccination such as generalized vaccinia, eczema vaccinatum, vaccinia necrosum, etc., are described only briefly. Although they are rare conditions, they are of great importance as iatrogenic diseases with a high mortality, and anyone who turns to Prof. Herrlich's monograph to find information on them will be disappointed not to find them discussed in greater detail. The section on animal pox diseases would also benefit from the inclusion of contagious dermatitis and lumpy skin disease. These are minor criticisms, however, and are only prompted by the high standard which the author has set himself. The book is beautifully produced and in appearance and scientific content is well worth its high price.

D. J. Bauer

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